VOLUME 18 NUMBER 2

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Archives of Dermatology and Syphilology

VOLUME 18 AUGUST, 1928 NUMBER 2

CHRONIC ATROPHIC LICHENOID DERMATITIS (CSILLAG)

SO-CALLED LICHEN ALBUS OF ZUMBUSCH *

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In 1914 in the *Journal of Cutaneous Diseases,* MacKee and Wise [1] published a paper on "white spot disease." The suggestion was made that certain peculiar forms of chronic eruptions did not seem to conform clinically with either lichen sclerosus of Hallopeau or with scleroderma guttata and white spot disease; they possibly represented transitional or intermediate dermatoses, presumably constituting a connecting link between these two disease groups. The majority of observers were in accord with this idea.

The types of eruption tentatively classed as intermediate or transitional were those which conformed more or less to the description of such cases as were published by Zumbusch, Csillag, Milian, Fischer, Vignolo-Lutati and others.[2]

Further experience, based on the study of personal cases and on those reported by other observers, has led us to believe that these aberrant dermatoses, instead of being transitional processes linking together two unrelated groups such as the lichens and the sclerodermas, are in reality examples of a separate and at times distinct disease entity.

SYNOPSIS OF THE LITERATURE

The original publications of Hallopeau and of Darier and the later ones of E. Hoffmann, Riecke, Herxheimer, Dreuw, Petges, Fischer, Milian, Bizzozero,[2] Alexander [3] and others in Europe, together with

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* Read before the Fiftieth Annual Meeting of the American Dermatological Association, Baltimore, May 12-14, 1927.

1. MacKee, George M., and Wise, Fred: White Spot Disease, J. Cutan. Dis. **32**:629, 1914.

2. Wise, Fred; and Rosen, I.: Further Observations on So-Called White Spot Disease or Sclerodermia Circumscripta, J. Cutan. Dis. **35**:66 (Feb.) 1917.

3. Alexander, Arthur: Der Lichen Sclerosus, Arch. f. Dermat. u. Syph. **121**:925, 1916.

the papers of Montgomery and Ormsby, and later, those of Ormsby, Fordyce, Hazen and others [4] in this country, in a measure served to clear the somewhat beclouded status of lichen sclerosus and its relation to different forms of scleroderma guttata and white spot disease. Today the accepted view is that Hallopeau's lichen sclerosus et atrophicus belongs to the lichen planus group, and that white spot disease is a form of scleroderma guttata.

On the other hand, few writers have expressed themselves with any conviction on the nosologic position of eruptions which seem to correspond in most particulars with the type described by Csillag under the title dermatitis lichenoides chronica atrophicans. Perusal of the literature indicates plainly that this variety of eruption has consistently been a stumbling-block in the path of those who have investigated this group of dermatoses and who have attempted nosologic classifications; it should be admitted here that we have tripped over the same stumbling-block in our own studies on the subject. The reason for this seems to be that too much importance has been attached to the variable microscopic observations in the various eruptions, the clinical features in many instances being relegated to a position of secondary importance. The need of discriminating between essentials and nonessentials appears to be particularly applicable to the study of the group of dermatoses under discussion.

The dermatoses which have been a source of confusion not only with respect to their clinical manifestations but also in connection with the interpretation of their histologic structures, are the following:

1. Lichen sclerosus et atrophicus (Hallopeau and Darier).
2. Lichen morphoeicus (Stowers).
3. Lichen planus atrophicus.
4. Lichen albus (Zumbusch).
5. White spot disease (Johnston and Sherwell).
6. Cardboard scleroderma (Unna).
7. Scleroderma guttata.
8. Lichenoid scleroderma associated with early atrophy.

Ormsby, whose interest in these eruptions is indicated by his publications, discusses this phase of the subject in his paper on lichen sclerosus; some of his quotations follow:

> Zumbusch's case of lichen albus is classed here as belonging to the Hallopeau type. Csillag's case of dermatitis lichenoides chronica atrophicans probably belongs here, as does Milian's case of lichen planus atrophicus, for which he thought the best title would be leukoderma with punctate atrophy. Riecke's case of provisional "white spot disease" practically fulfils the requirements of this group. . . . Csillag describes a case which he classes as analogous with Zum-

4. Feldman, Samuel: Lichen Planus et acuminatus atrophicans, Arch. Dermat. & Syph. **5**:102, 1922.

> busch's lichen albus. The clinical description of the lesions in this patient correspond in many particulars to those found in the cases of the subject under discussion, and is therefore placed provisionally in this group. . . . Milian describes a case under the title of lichen planus atrophicus in which pinhead to pea-sized white lesions occurred. . . . In the discussion of this case Darier stated that the disorder could be classed in one of four categories: lichen planus sclerosus, white spot disease, cardboard scleroderma of Unna, or lichen albus.

From this statement by Darier it must be assumed that he does not regard lichen sclerosus and lichen albus as being identical diseases; with this expression of opinion from an observer of his knowledge and experience, we establish contact with one of the "high spots" in the controversy: five different diagnoses are suggested as being applicable to one and the same eruption, presented with the designation lichen planus atrophicus.

Zumbusch published his case of lichen albus as a "hitherto undescribed dermatosis," but Hallopeau regarded the eruption as an example of lichen planus sclerosus. Ormsby is inclined to agree with this view.

Csillag regarded the eruption in the case he described as being analogous to that of Zumbusch, and believed that it bore no relation to any form of lichen planus. Histologically, the changes in his case resembled those observed in certain cases of circumscribed scleroderma and lichen sclerosus.

In Riecke's study of the subject, he described a case which he called white spot disease; he classified it with Westberg's and with Johnston and Sherwell's cases. On the basis of his clinical and histologic descriptions, fortified by illustrations of the eruption, Ormsby is inclined to group it with lichen planus sclerosus. Riecke's case demonstrates the fact that some of these eruptions are variously diagnosed not only on the basis of their clinical manifestations, but even on the presumably more solid foundations of microscopic observations.

Fordyce reported a case which resembled white spot disease clinically, but the histologic observations were similar to those of lichen sclerosus, so that he was led to conclude that "histologically the condition might be looked on as a sclerosis, but in connection with the clinical manifestations it is more rational to consider it an atrophy."

In Fischer's patient, the eruption resembled Zumbusch's description of lichen albus, but the microscopic changes conformed with those described in Unna's cardboard scleroderma. Fischer classes such cases as those of Zumbusch, Csillag, E. Hoffmann and Milian with the sclerodermas. Hallopeau believes that the cases of Zumbusch and Milian are examples of lichen sclerosus. Riecke relegates the cases of Zumbusch and Csillag to the sclerodermas, and that of E. Hoffmann to

lichen sclerosus, while Hoffmann himself interprets his own case as a scleroderma.

In an analysis of the subject by Bizzozero, the cases of Zumbusch, Csillag, Fischer and Vignolo-Lutati are classified as belonging to the group of lichenoid sclerodermas.

The crux of the situation is expressed by Fischer when he says that if one regards these various types of eruption as a whole, it is practically impossible to classify them on the basis of the pathologic changes alone. Eruptions apparently belonging to the lichen planus group, like those of Hallopeau, Ormsby, Hoffmann, Alexander and others, present histologic pictures which at one stage or another in the evolution of the lesions conform with the microscopic changes observed in eruptions which clinically are not related to the lichen planus family, as in the cases of Zumbusch, Csillag and Milian. Broadly speaking, these histologic alterations often correspond to those seen in different varieties of guttate scleroderma. In many of them there is degeneration of the connective tissue with disappearance of the elastica, a process foreign to lichen planus.

From this brief review it may be readily inferred that the diagnosis of this class of eruptions, which, as Jadassohn remarked, seem to bear some sort of kinship to atypical scleroderma on one hand and to lichen planus on the other, is fraught with difficulties, even in those instances in which the clinical picture is partly interpreted by the microscopic observations.

We regard the following case as an example of chronic atrophic lichenoid dermatitis. In 1912, the patient consulted the late Dr. Haase of Memphis, who diagnosed the eruption as white spot disease. A year later she became a patient of Dr. Shelmire, Sr., in Dallas. In 1926, one of us (F. W.) had the opportunity of examining the patient while attending the Dallas meeting of the American Medical Association. Dr. Shelmire has permitted us to publish a report of the case.

REPORT OF CASES

CASE 1.—*History.*—Mrs. R. M., white, aged 68, was born in America, of German parentage. She was a normal, full term infant, and had had the ordinary diseases of childhood. At the age of 18 she had typhoid fever and at 48, pneumonia. She had chickenpox when a child, but scarring did not result. Her husband was living and well. She had not been pregnant. The menses were normal. Menopause occurred at the age of 45.

Physical Examination.—The patient was slightly obese. The organs of special sense were normal. The teeth were replaced by artificial plates. She did not have an eruption on the buccal mucosae. There was slight emphysema of the chest, with a few moist râles at the base. The heart showed a left-sided hypertrophy. The visceral and glandular organs were normal.

The patient said that until May, 1912, her skin had always been normal. Toward the end of this month she noticed "some twenty or thirty hard, white

pimples" on the flexor surfaces of the wrists and forearms. Individual pea-sized papules were separated by areas of normal skin. The family physician, whom she consulted, diagnosed this condition as pellagra. There was slight itching of the affected areas of the skin. Three months later, papules appeared on the back, on the front of the neck and on the upper part of the chest. She then consulted Dr. Haase, who made the diagnose of white spot disease and removed a section for microscopic study. She gave a negative reaction to the Wassermann test. In November, 1913, this patient was seen by Dr. Shelmire, Sr. Because of the innumerable white papules simulating those of lichen planus in configuration but not in color, he made a diagnosis of lichen planus atrophicus. On November 12, the following notation was made on the history card: "Patient has statement from Dr. Haase that he diagnosed the condition as white spot disease. No lichen planus papules visible on any part of the body. Mucous membranes free of lesions. Itching absent." At the time of this statement, the eruption was more extensive than when the patient was seen by Haase, as it now implicated the skin of the forearms, neck, upper part of the chest, breasts and upper portion of the back. According to Shelmire, Sr., who has followed this case for the past fourteen years, the lesions presented today are exactly the same as they were fourteen years ago, except that the eruption has become more extensive, invading the skin of the upper extremities, abdomen, entire back and gluteal regions; the number of individual lesions has increased threefold.

Present Condition.—The patient presented a generalized, well defined eruption which affected the skin of the upper portion of the extremities, the entire torso, gluteal regions and upper third of the thighs. At first glance, the eruption seemed to be made up of achromatic papules, scattered and closely studded together, suggestive of generalized lichen planus. On closer scrutiny, this first impression is banished. The eruption consisted of three types of lesions: achromatic papules, linear or striate configurations and dollar to palm-sized and larger plaques. It is evident that these larger and later lesions were but end-results of the former lesions, for the striate lesions and plaques were composed of individual, closely agminated papules, which, even in such close proximity, had not lost their individual characteristics.

On the abdomen and on the lower part of the back, the papular lesions were ivory-white and yellowish. The older lesions on the neck and on the upper portion of the chest were almost a dead white, simulating the color of white spot disease, and varied in size from that of a match head to that of a pea. These lesions were flat-topped, oval and round, and irregular in outline. Some of the larger papules had depressed centers. When viewed from the side, these pea-sized and larger papules with depressed centers and elevated borders gave the appearance of being annular. Most of the papules, which numbered several thousands, were distinctly elevated, some of them as much as 1 mm. above the surrounding skin; others could be barely felt by the palpating finger, to which they imparted a feeling as of induration. Their surfaces were flat and glistening; some had elevated borders, thus simulating delling; horny plugs, true dell formations, punctiform depressions and cross-hatching were not noted. Scaling was absent, but branny scaling could be produced by scratching the older papules on the upper portion of the chest and on the neck. Of the thousands of papules there were only about a hundred which had a distinct border. Surrounding some of the larger papules was a delicate rosy areola, while around others this halo was distinctly hyperpigmented. The surfaces of the yellowish-white lesions, which seemed to be the most recent, were smooth. The older

papules on the neck presented a distinct wrinkling of their surfaces, suggestive of superficial atrophy. On the forearms and on scattered areas on the trunk there were barely palpable, nonelevated lesions with atrophic surfaces.

The linear lesions were scattered over the entire affected area, but were most pronounced on the shoulders, neck and lower portion of the abdomen; they were from about 1 to 2 inches (2.5 to 5 cm.) in length, with the width of the individual papular elements. These linear lesions were elevated, as were the papules,

Fig. 1 (case 1).—A generalized eruption which consists of lichenoid papules, areas of pigmentation and atrophy of the skin of the breasts.

and on palpation they gave the same sensation of resistance; between them, the skin appeared to be normal. On the lower part of the abdomen, they seemed to follow the lines of cleavage of the skin, while in other regions they ran transversely. In some areas, as on the abdomen, the linear formations joined, forming a sort of meshwork. The most important feature about them was that they were made up of closely approximated papules, which were juxta-apposed, but not confluent. Although this description seems to indicate linear lichen planus, the actual appearance of the lesions did not suggest that disease.

The plaque lesions were formed by the close approximation of papules. They varied in size from half an inch to the palm of a man's hand or larger. The smaller plaques were scattered diffusely over the entire affected area of diseased skin, while the larger plaques were confined to the middle and upper portions of the back and to the breasts. These plaques were elevated, and those on the breasts presented distinct atrophy.

The skin of the lower portions of the breasts in their entire circumference was parchment-like, with fine wrinkling and loss of cutaneous elasticity. The

Fig. 2 (case 1).—A generalized eruption which consists of lichenoid papules, areas of pigmentation and atrophy of the skin of the breasts.

point of a needle when introduced under the epidermis could be rotated between it and the derma, as though a space existed between the two layers of the skin. Here the skin was smooth, soft, white and glistening. Telangiectases were absent. Scattered over this parchment-like skin on the breasts were pea-sized areas of normal colored skin, with here and there a dense, elevated, papular lesion. When a needle which had been inserted into this parchment-like epidermis was removed, a drop of serum exuded from the punctured wound. Other punctured spots remained dry.

Fig. 3 (case 1).—Sclerosis of the connective tissue and thinning of the epidermis (Van Gieson stain).

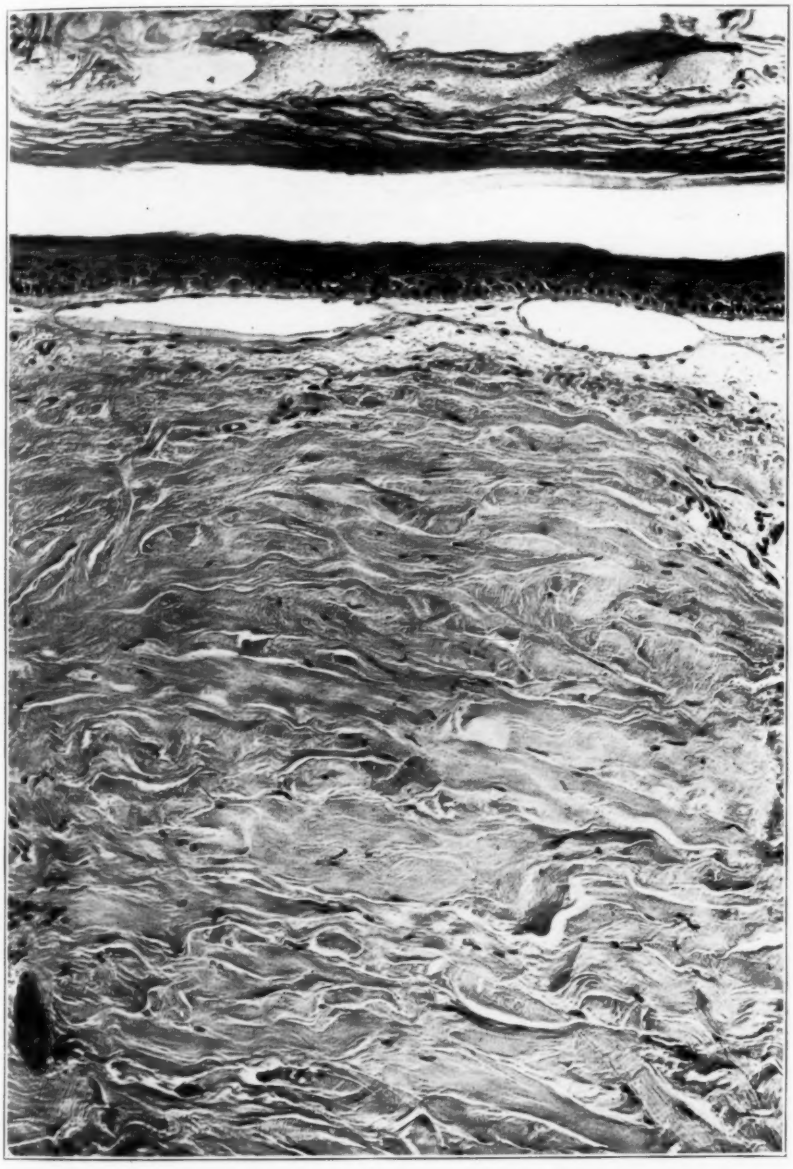

Fig. 4 (case 1).—Hypertrophy of the collagen, with early collastin degeneration; thinning of the epidermis, and dilatation of the subepidermic lymph-spaces (Van Gieson stain).

The plaques were free from scales, horny plugs, follicular depressions, cross-hatching, telangiectases and lanugo hairs. Between some of the plaques were areas of what appeared to be areas of normal skin.

From the clinical standpoint, none of these different lesions would give one the impression of being a form of scleroderma, either in its early stages or in its late atrophying phase.

Microscopic Examination.—The section removed from the lumbar region, a little to the left of the spine, consisted of a lentil-sized papule. The section was fixed in Bouin's solution.

The outstanding features of the section were: a pronounced condensation of the connective tissue of the corium, with collastin degeneration; absence of the adnexa of the skin; few and widely separated blood vessels; a thinned epidermis; absence of rete pegs and papillary bodies; edematous connective tissue and collagen bundles disposed in a loose meshwork in the subepidermic zone.

The horny layer was lamellated and separated from the underlying cells by a broad space. Parakeratosis was absent, unless indicated by the absence of the stratum lucidum, a diminution in the number of layers of the prickle cell stratum and the condensation and shrinkage of some of the prickle cell nuclei. The granular layer was from one to four strata wide. The basal cell layer was represented by a straight line, the palisade cells, in the greater part of the section, formed a well defined boundary against the upper border of the cutis, but over those portions of the corium where the collagen bundles were loosely meshed, there was a partial disorganization of the basal cell layer. Evidence of parenchymatous or interstitial edema was lacking.

In the corium there was a generalized hypertrophy of the collagenous bundles, most pronounced in the fibers composing the lower or coarse collagen layers. In the subepidemic portion of the corium, the collagen bundles were densely packed. In the zone of loose collagen formation, the connective tissue showed evidence of granular degeneration, while the rest of the tissue had undergone a collastin degeneration. The cellular elements were few; there were a few fibroblastic and scattered connective tissue cells.

The vessels of the corium were narrowed, and the appendages, the coil glands and ducts, hair follicles and sebaceous glands were absent; only remnants of these structures persisted.

The finely reticular papillary and subpapillary layers had been replaced by coarse hypertrophied bundles of collagen lying in close apposition to the basal cell layer. Sclerosis was pronounced.

In the remains of the subepidermic zone were a number of dilated lymph vessels and isolated dilated capillaries with distinct endothelial proliferation. The walls of the blood vessels deeper down were edematous, but in them connective tissue proliferation did not occur.

The elastic tissue, except in the subepidermic portion of the corium, had undergone little alteration and appeared to be practically normal. But within the subepidermic zone, the elastica was fragmented, granular, clumped and in places entirely absent.

Summary.—The section showed thinning of the epidermis and absence of rete pegs and papillary bodies, apparently due to sclerosis of the collagenous bundles in the corium. In the latter, the zone of loose collagenous formation had undergone granular degeneration, while the other portions of the corium exhibited a collastin degeneration. The upper layers of the elastic tissue also showed a degenerative process. The process as a whole was evidently a sclerosis undergoing degeneration and terminating in atrophy.

CASE 2.—*History.*—Mrs. S. G., aged 29, born in Russia, had been a resident of this country for eleven years. She said that the eruption on her skin had first appeared three months prior to consultation, but judging from the character of the eruption, this shortness of duration seemed doubtful. General examination of the patient did not reveal any abnormalities, and she gave a negative reaction to the Wassermann test. She had had one miscarriage; three children were healthy; one child died of pulmonary tuberculosis.

The lesions occupied the upper part of the wall of the chest, the clavicular regions and the sides of the neck; there were two dollar-sized plaques on the back,

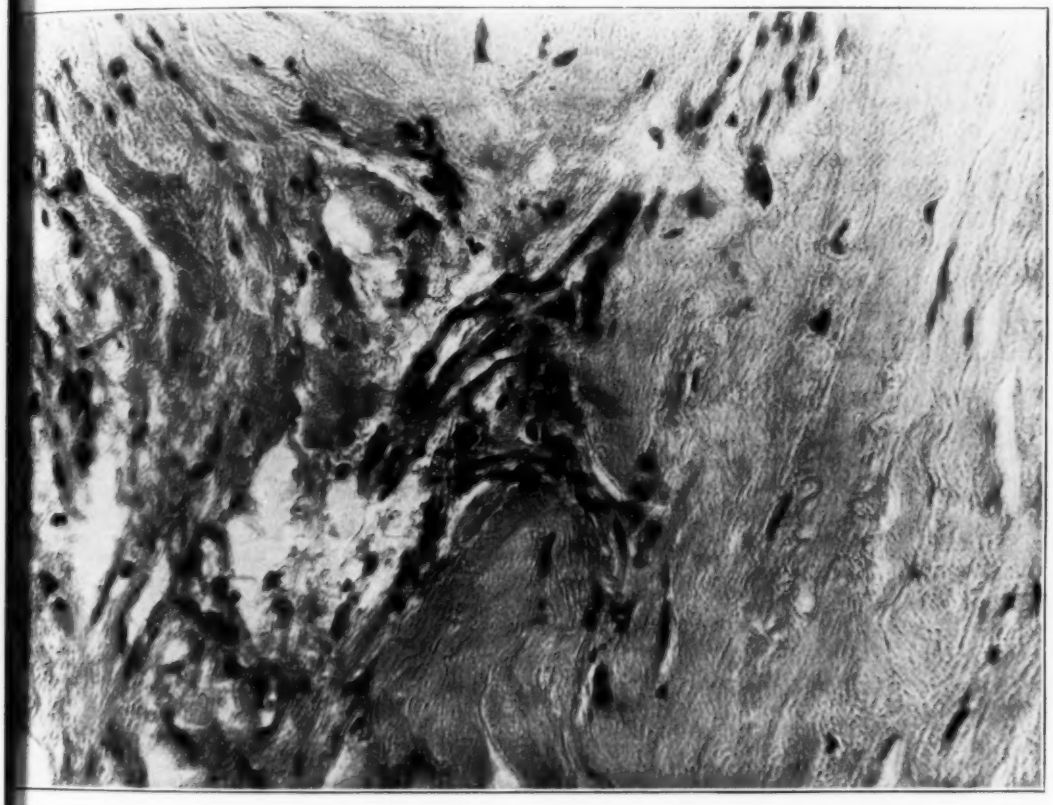

Fig. 5 (case 1).—Granular degeneration of the collagen and edema of the vessel walls (hematoxylin-eosin stain).

one situated over the right scapula, the other approximately over the last cervical vertebra. On the anterior aspect of the right wrist were two isolated papular lesions. The buccal mucosae were free from lesions and were healthy in appearance.

Although the patient said that she had not noticed an eruption until three months before, the changes in the skin gave the impression of being much older —probably a year or more. The question as to whether she ever had had an eruption of lichen planus was carefully considered, and was definitely answered in the negative.

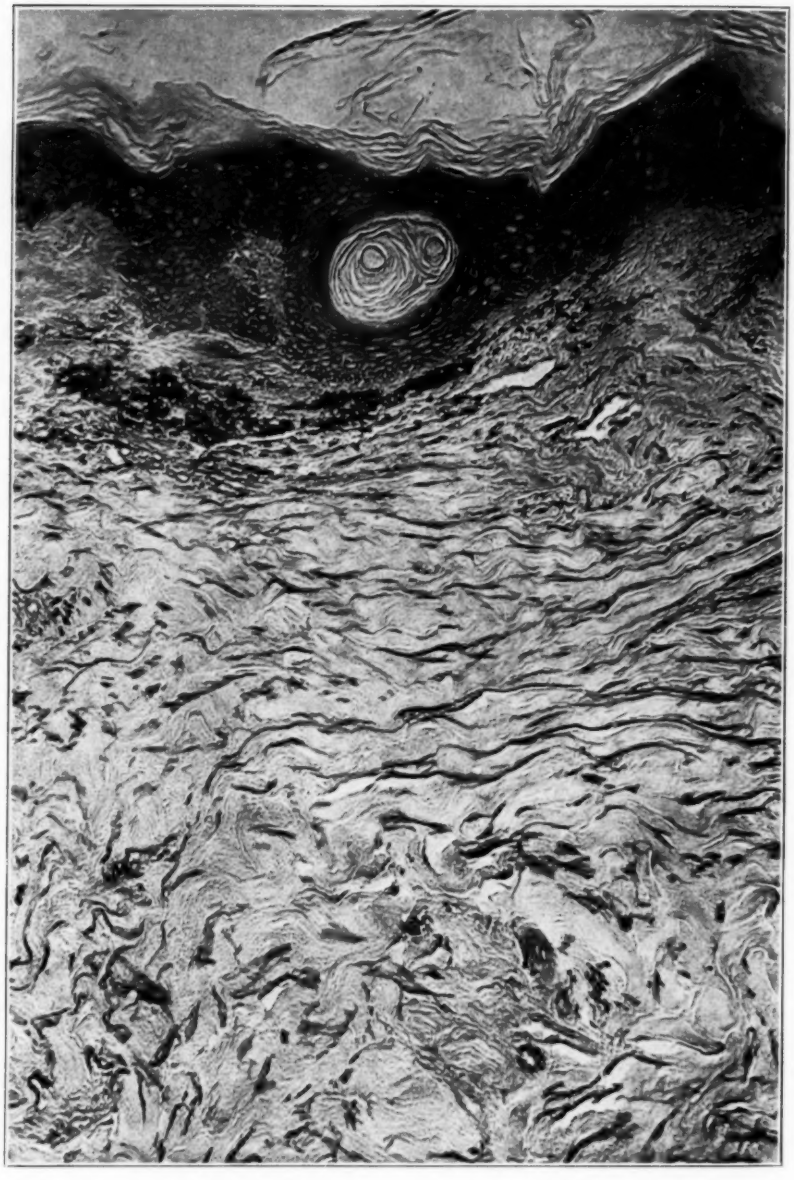

Fig. 6 (case 1).—Fragmentation, granulation, clumping and absence of elastic tissue fibers in subepidermic zone (Weigert stain).

The lesion on the chest was a horseshoe-shaped formation, its curved portion lying over the sternum and the lateral parts over the clavicles and extending up to the sides of the neck. The edges of this plaque were ill defined, merging with the adjacent normal skin, except the two ends of the horseshoe, which occupied the hollows of the shoulders; here the edge of the lesion was sharply defined against the normal skin on the sides of the neck. The surface of this plaque was smooth and distinctly glistening; the color was mottled, some parts were ivory white, other parts yellow, with broad areas of brownish-yellow pigment irregularly distributed over the entire suface. Close inspection revealed that the plaque was formed by the coalescence of flat, shiny papules, varying in size from that of a pinhead to that of a lentil, which were slightly elevated. For the most part, these papules formed a mosaic; but in three areas, one over the left clavicle, another just beneath the right clavicle and the third to the right of the sternum, the coalescence of the papules had resulted in irregularly shaped, smooth, white, glistening, waxy-looking atrophic patches, the surfaces of which resembled wrinkled cigaret paper.

The majority of the individual papules were surrounded by a distinct ring of hyperpigmentation, while a number of the more outlying papules at the concavity and convexity of the horseshoe presented well defined delicate areolae of violaceous tint. In passing one's finger over a patch of these papules, one did not get the sensation of a surface studded with papules, but rather that of a smooth surface; but if the skin were closely viewed in a proper light from the side, the slightly uneven papular surface could be plainly seen. There were no horny plugs, central depressions or evidence of cross-hatching.

The two plaques on the back were sharply defined, discoid lesions; the edges were deeply pigmented by a brownish-yellow zone, about one-eighth inch in width; the surfaces were smooth to the touch, soft, velvety and easily wrinkled by the slightest pressure of the finger; their color was a mottled brown. Only the faintest evidence of papule formation was visible in these plaques, the inference being that the coalescence and subsequent flattening of the papules had resulted in a smooth, atrophic surface.

The two papules on the right wrist were about one eighth of an inch in diameter, slightly elevated above the surrounding normal skin; the surfaces were waxy-yellow, smooth and glistening; their consistence was hard; there was an absence of pigment or a violaceous ring at their peripheries.

Itching and other subjective symptoms were absent.

The patient would not permit a section to be removed from the lesions on the trunk, but submitted to a biopsy of one of the papules on the flexor surface of the right wrist.

This patient was exhibited before several local dermatologic societies in which the question of differential diagnosis between white spot disease, lichen atrophicus and atrophying scleroderma was fully discussed. The diagnosis of chronic atrophic lichenoid dermatitis was made by the majority of those who examined the lesions, among them being Fordyce, Pollitzer, MacKee and Williams.

Microscopic Examination.—The section was taken from the anterior surface of the right wrist and consisted of a lentil-sized, flat, white papule. It was fixed in Bouin's solution.

The outstanding features of the section were: a condensation of the collagen bundles, most pronounced in the lower cutis, with scattered bands in the midcutis. The midcutis and deep cutis presented a moderate grade of interstitial and parenchymatous edema. In the midcutis, there was a light grade of perivascular infiltration. The epidermis in its greater portion was little altered.

The papillary bodies and rete pegs were fairly well defined. In the upper cutis, there was a moderate dilatation of the lymphatics and capillaries.

With the exception of some basal cell disorganization which occurred in scattered foci, noteworthy changes had not occurred in the epidermis. The granular layer was normal; the prickle cell layer, especially in one portion of the section, showed considerable thinning. The palisade layer formed an irregular

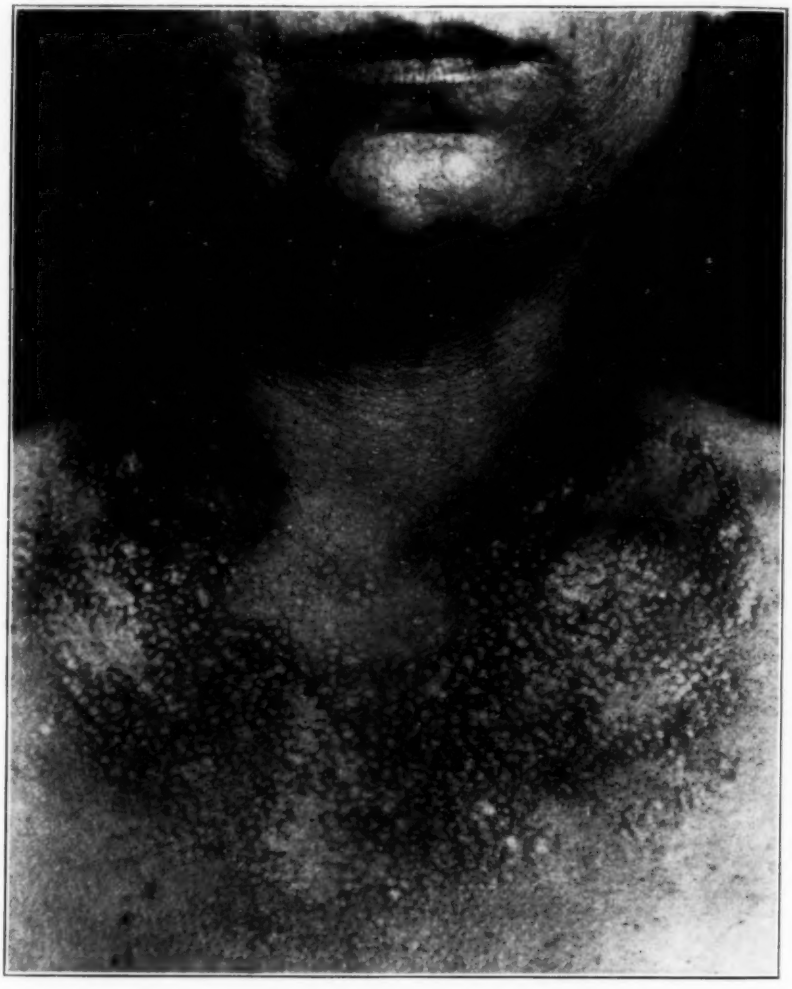

Fig. 7 (case 2).—A horseshoe-shaped patch which consists of juxta-apposed papules, areas of pigmentation and atrophic plaques of the skin.

wavy line, well defined against the underlying derma. The interpapillary pegs had for the most part been flattened.

In the upper portion of the corium, the collagen bundles were compressed and homogeneous. Scattered throughout were a number of dilated lymph spaces and small blood vessels, with endothelial proliferation. In the lower corium, the collagen bundles were somewhat homogeneous in appearance, unevenly stained and

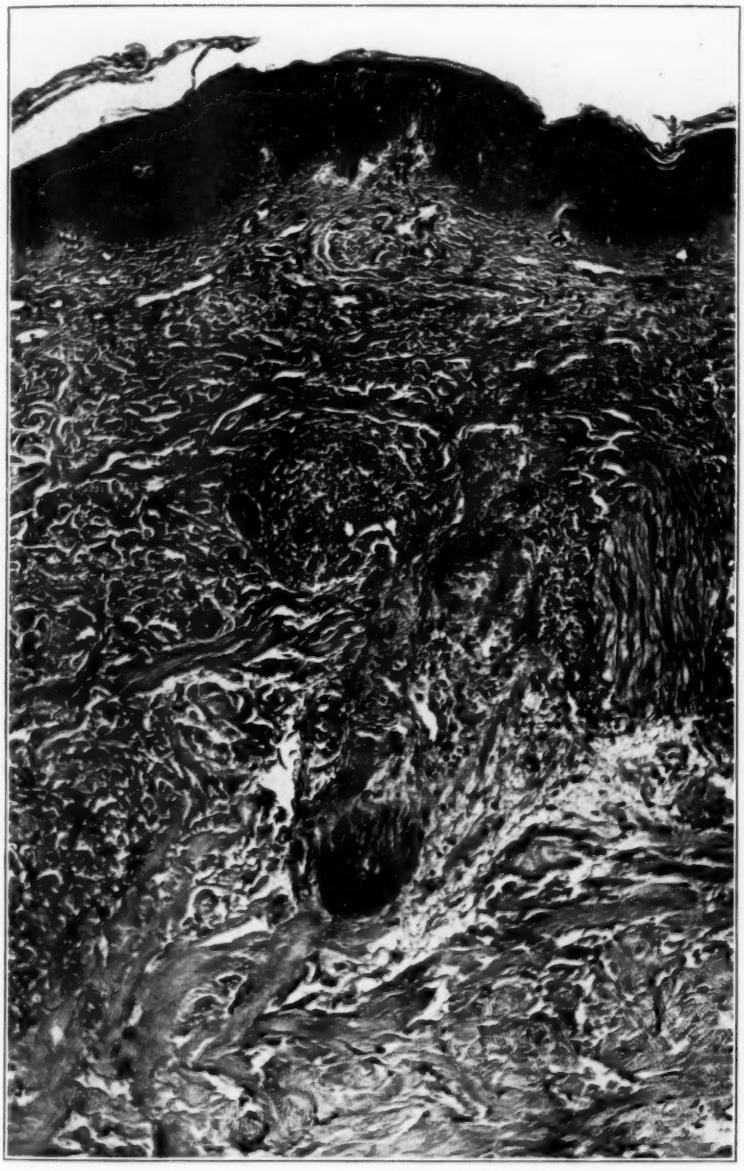

Fig. 8 (case 2).—Condensation of collagen bundles, edema of the cutis and perivascular infiltration, and dilatation of the lymphatics and capillaries (hematoxylin-eosin stain).

showed evidence of collastin degeneration in their somewhat glassy appearance. The collagen in the subepidermic portion showed the beginning of a granular degeneration in scattered foci. There were a few large fixed connective tissue cells and a sparse number of fibroblastic elements. The vessels in the subepidermic zone were dilated and exhibited distinct endothelial proliferation. The walls of the deeper vessels were edematous.

The perivascular lymphatic spaces of the vessels in the midcutis were moderately dilated and contained few lymphocytes; in one area there was a widely dilated space which contained many densely packed lymphocytes and a few larger, fixed connective tissue cells. A similar zone of perivascular infiltration occurred in the deep cutis. Remnants of a compressed hair follicle and arrector pili muscle were situated in the midcutis. The entire corium presented a pronounced sclerotic appearance.

The elastic tissue as a whole had not undergone pronounced alterations. In the deeper portion of the cutis, the fibers appeared to be practically normal; in the midcutis there were evidences of structural changes, manifested by fragmentation, distortion and areas of complete disintegration of the fibers; in the subepidermal portion, there were areas in which the elastic fibers showed clumping and structural degeneration; in spots where the basal cell membrane was disorganized, the elastica had disappeared entirely.

Summary.—The section as a whole may be interpreted as one presenting a long-standing exudative inflammatory process, with early degeneration of the collagenous tissue, leaving the epidermis comparatively unaffected. The elastica had taken part in the process, as evidenced by its structural alterations and its absence in certain portions of the corium.

OUTLINE OF THE CLINICAL FEATURES

Chronic atrophic lichenoid dermatitis is characterized by the formation of a varying number of white, shiny, indurated, round and oval, well defined papules appearing in closely agminated groups of individual lesions. These papules are in juxta-apposition, but they do not coalesce; that is, they do not blend together to form larger patches. The papules may have no areolae; or there may be a faint pink peripheral zone or more frequently a zone of hyperpigmentation. Scaling and Wickham's striae are absent; the buccal mucosae and the skin of the genitalia are not attacked. Some of the papules have shallow depressions, but the true dell formation seen in lichen planus is absent. The lesions do not itch. Punctate depressions, horny plugs and cross-hatching do not play a part in their evolution.

Following the full development of the papules, a flattening and superficial shrinking takes place, so that the outlines of the papules become less distinct, but are not obliterated; the close approximation of several dozen or several hundreds of flattened papules results in the formation of a smooth, glossy patch of round, oval or irregular outline, and of varying extent. The periphery of such a patch is usually hyperpigmented. A faint degree of resistance is imparted to the finger when these plaques are palpated. In the patches of longest standing and greater extent, the surface is smooth, more or less wrinkled, and the

skin is soft and dead white. Some of these individual patches finally coalesce to form large areas of atrophic skin.

The different stages of evolution may be present in the same eruption at the same time: fully developed papules with well defined peripheries, crops of agminated flattened lesions forming circumscribed patches and areas of skin undergoing pronounced atrophy with wrinkling of the surface.

DIFFERENTIAL DIAGNOSIS

Differentiation of the various members of this group of dermatoses, if based solely on their histologic alterations, has been found impracticable, as pointed out by Fischer, Bizzozero, Fordyce and others.

One reason for this fact is that if one considers the four conditions which are the most readily recognizable on the basis of their clinical features, namely, lichen sclerosus, scleroderma guttata, white spot disease and lichenoid scleroderma, it is found that they have several characteristics in common. In each of them the lesions develop slowly and insidiously; they undergo evolutionary changes which are often analogous and sometimes indistinguishable under the microscope; they exhibit different shades of color ranging from ivory yellow to snow white; the surface of the lesions may be dull, like that of ground glass, or shiny like wax, or glistening like mother-of-pearl. Scaling, cross-hatching, punctate depressions and horny plugs may be present in some and absent in others. The elementary lesions may be isolated in one instance and grouped and confluent in another. Only the presence of genuine lichen planus lesions, confirmed by microscopic examination, definitely distinguishes one of Hallopeau's two varieties of lichen sclerosus from the other three dermatoses mentioned. Atrophy may occur in all of them.

The resemblances in histologic structure have been pointed out in a preceding paper (Wise and Rosen)[2], in which it was stated that "Variations in the microscopic appearances are due to differences in the intensity of the process, in the age of the lesion, the region from which biopsies were obtained, and so forth."

The following microscopic comparisons were made in the papers by Wise and Rosen: The chief microscopic changes in lichen sclerosus, as first described by Darier, are as follows: thickening of the horny layer, with prolongations into the follicles and sweat gland orifices; thinning of the malpighian layer with disappearance of interpapillary pegs and corresponding absence of papillae; sclerosis of the papillary bodies and upper portion of the corium, where the connective tissue bundles are compact and poor in cellular elements, the capillaries showing dilatation here and compression there, the elastic fibers attenuated; an aggregation of grouped round cells, just beneath the sclerotic zone; a sparse collection of cells about the sweat glands and some of the blood vessels.

In cardboard scleroderma, the microscopic appearances resemble each other in practically all of the cases which have come under examination in the advanced

stages of the disease. These changes consist of: hypertrophy of the horny layer; thinning of the malpighian layer; the presence of clefts and lacunae varying in shape and size, between epidermis and corium; sclerosis of the papillae and upper portion of the cutis, the connective tissue bundles being disposed in parallel horizontal strata, between which are seen only the faintest lines of separation; a paucity of cellular elements and elastic fibers in the corium; a grouped infiltration, consisting chiefly of lymphoid and spindle cells, bordering the sclerotic margin below.

Evidently, the histologic changes in both conditions bear many points of resemblance. In lichen sclerosus, the subpapillary infiltrate gradually invades the deeper portions of the corium, leaving in its place a zone of sclerotic tissue, which grows correspondingly in width. A similar process takes place in cardboard scleroderma. After the initial stage of inflammatory edema, involving the papillary and subpapillary regions, there follows the stage of collagenous hypertrophy, which, in turn, is succeeded by the sclerosis. The infiltration gradually disappears from the area originally involved, becoming localized at the periphery of the lesion, while the indistinctly separated bundles of connective tissue are replaced by a compact mass of collagen. Comparing these microscopic changes with those seen in our own case of lichenoid scleroderma, we find that the end-stages of these different varieties of guttate scleroderma are almost identical, the chief difference being in the absence of a zone of peripheral inflammatory cells in our case. These are in brief the microscopic changes discussed in the previous paper.

In connection with the microscopic changes, it has been pointed out that these are analogous to those observed in certain evolutionary phases of lichenoid scleroderma. It is of interest to note that the late Professor Kyrle, on the basis of his microscopic studies, did not regard scleroderma and white spot disease as identical morbid processes. He called attention to the fact that despite their clinical identity, he believed that certain alterations in the elastica in white spot disease, leading to its disintegration and final disappearance, were due to destructive agents not present in true scleroderma. In his judgment, the collagenous tissue is primarily attacked by the pathogenetic agent in scleroderma, leaving the elastica relatively unharmed; in white spot disease, he thought these conditions were reversed. From these observations he believed white spot disease to be genetically different from scleroderma, and that the former bears a much closer relationship to idiopathic atrophy than it does to scleroderma. He suggested that the relationship between white spot disease and circumscribed macular atrophy was analogous to that existing between the flaccid and the firm variants of the diffuse form of acrodermatitis atrophicans.

These observations are of interest so far as they apply to the end-stages of chronic lichenoid dermatitis—atrophy with concomitant loss of elastic tissue. Assuming that the condition most closely simulates lichenoid scleroderma and white spot disease, in both of which the final stage of evolution is atrophy, it seems justifiable to conclude that

differentiation must rest on clinical, not on histologic, observations This applies practically to the entire group of dermatoses under discussion, with the exception of genuine lichen planus sclerosus in its earlier stages.

SUMMARY AND CONCLUSIONS

If we sum up and correlate the diverse clinical and microscopic features of the different eruptions belonging to the group under discussion as they appear in the literature, and regard the whole group from a broad point of view, we are led to form the following conclusions:

The various dermatoses permit a clinical classification on the basis of their gross cutaneous manifestations, under three heads: (1) those which show kinship to scleroderma or morphea; (2) those which show kinship to lichen planus, and (3) those which show kinship neither to scleroderma in the literal clinical sense of scleroderma, implying "hard skin," nor to any form of lichen planus; the last group, instead of representing a transmutation of one type of disease to the other, is in reality a distinct clinical entity.

The two cases described were subjected to careful differential diagnostic consideration under the eyes of expert clinicians whose opinions coincided with those already expressed by us, that is, that from the clinical standpoint neither of the two eruptions could be properly grouped with lichen planus sclerosus, white spot disease or scleroderma. Histologically, the changes in both eruptions closely resemble those seen in so-called lichenoid scleroderma, a fact pointed out by Fordyce, Bizzozero and other observers.

As to its designation, we are inclined to approve of the term suggested by Csillag—dermatitis lichenoides chronica atrophicans—which, although long and unwieldly, removes and sets it apart from the other groups and indicates and stresses the clinical features of the eruption.

In publications of society transactions, one frequently encounters protests voiced against the use of the adjective "lichenoid" when applied to dermatoses unrelated to lichen planus on the assumption that the word is prone to give rise to confusion in the mind of the student, causing him to visualize a lichen planus-like eruption. Against this restriction one might argue that the adjective "ovoid" be eliminated from the vocabulary of scientists, for fear of its bringing to the student's mind the picture of an egg. As the disease is extremely rare, it is hoped that the occasional use of its long name will not prove to be onerous.

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ABSTRACT OF DISCUSSION OF PAPER BY DR. SHELMIRE AND DR. WISE

DR. J. B. SHELMIRE: The lesions on the back of this patient as Dr. Wise states were not caused by biopsies; they were basal cell carcinomas. There were three small basal cell carcinomas that were cauterized and treated with radium. I am glad that he called attention to these lesions, for it is extremely rare for a cancer to develop on a scleroderma. When this patient first came under my observation fourteen years ago, I was reluctant to change the diagnosis of white spot disease made by Dr. Haase. When she came back later, I looked up her record and found that I had put a question mark after the white spot disease, and changed it to lichen planus atrophicus. Several prominent dermatologists had seen this patient, and all were of the opinion that it was a type of scleroderma or lichen planus. I congratulate Dr. Wise for having taken up the case and properly classified it.

DR. ORMSBY, Chicago: I should like to say that when one attempts to analyze a group of cases from a description in the literature one is at a disadvantage, and the classification we made a number of years ago was not complete and would in time have to be changed. Even the cases described fully are not satisfactory, for, as Dr. Wise says, one has to see a patient to realize the difference in the description and the real condition. When we first did this work about 1906, there was the same confusion that exists now. We believed that these cases could all be put into two categories, lichen planus sclerosis et atrophicus and morphea guttata, and in a paper written four years later, I still held that belief. Since then I have seen many more cases and have been able to put not all, but most of them, into one or the other of these groups. I saw the patient described by Dr. Wise when I was in Dallas last year, and my opinion was that it was a case of lichen planus atrophicus et sclerosis, although I was a little doubtful of this diagnosis. All of the other cases I have seen I have been satisfied came within the two groups mentioned. From the histologic changes which have taken place in this case, which I did not see at Dallas, there is no question that the condition is neither lichen planus atrophicus et sclerosis nor morphea guttata, and I agree with Dr. Wise that it should be considered a separate entity. The name given by Csillag is acceptable because it really describes the condition.

I have had interesting experiences in some of these cases, one of which I should like to describe. A patient who had typical lichen planus sclerosus et atrophicus under observation twenty years ago had the lesions in the usual location, over the shoulders and the clavicles, and she recovered within a few years. Fifteen years later, I saw her with a typical patch of ordinary morphea on the abdomen. There was no connection between the two disorders, each being classic in its type. Had the two conditions been present at the same time, confusion might have occurred.

I have seen one patient with a generalized eruption of lichen planus sclerosus et atrophicus. In this case the disorder underwent involution after a time, but the case of Dr. Shelmire, which Dr. Wise has reported, has perisisted over a period of several years.

I believe that the chief point of distinction between the disorder described by Dr. Wise and lichen planus atrophicus is in the presence in the latter of horny plugs and the horny cavities that are left after the plugs fall. If these are present, one can be practically certain of the diagnosis; if they are absent, the case belongs in one of the other two groups.

DR. POLLITZER, New York: I have had an opportunity of reading this paper before and of studying two cases, one that began about two and a half years before I saw the patient. A young man had a plaque on the posterior aspect of the wrist and one above the elbow on the same arm. The case seemed to correspond precisely to that described by Csillag and published in Jacobi's "Atlas." This patient was also seen by Dr. Wise. I examined a specimen from this patient, and it was my conclusion that the process was scleroderma. It had, to my mind, all the histologic characteristics of that disorder.

I saw another case about six months ago that I think was the same disease at its earliest inception. I do not think that any case has been observed earlier than this. The patient was a young man with a little patch of papules just above the left nipple. He said that while using a towel he had noticed a little thickening at this point and on examining it had found that there was some discoloration. There was a patch about an inch and a half long and somewhat less in width that had the appearance of a beginning scleroderma. There was no marked violaceous border, but the entire area was faintly violaceous. Over the surface there were little white spots that at first glance suggested lichen planus in contour and size, but they were not elevated. The lesion was flat and on palpation gave one the impression of a doughy mass. I saw the patient again last week and there did not appear to be any change. There is no suggestion of lichen planus; the whitish spots are still white.

I agree that this disease does not correspond precisely with any of the conditions that have been mentioned in the discussion. At the same time, I do not think that there is any question but that it is a form of circumscribed scleroderma. The elevated papules, with definite borders, horny plugs, etc., which occur later are a secondary process and are, I believe, the consequence of a sclerotic process in the cutis which for some reason is not so evenly distributed throughout the affected area as in ordinary scleroderma, with the result that little islands are formed which are different from the rest of the tissue involved. Whether this condition merits a special name to indicate a special variety I am not sure, for I think it is a form of scleroderma, but at the same time that modification, it may be conceded, may merit a special name.

Dr. Wise: This study was inspired by the fact that perhaps once or twice a year we run across cases in New York which cannot be identified as either lichen planus atrophicus et sclerosus of Hallopeau or as any form of scleroderma. The name given by Csillag was thought to be the best. I have observed six other cases that come within this provisional category. I agree with the statements made by Dr. Ormsby and Dr. Pollitzer that we are probably dealing with an aberrant form of scleroderma; but there are certain features that are not distinctly characteristic of scleroderma, particularly with reference to the changes in the elastic tissue in Csillag's disease, as pointed out by Kyrle.

TATTOO AND SYPHILIS *

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The literature of the last half of the nineteenth century contains many reports of syphilitic infection implanted during tattooing, sometimes in epidemic form, as brought out by Maury and Dulles.[1] However, only after the beginning of the twentieth century does one find reports of an unusual distribution of the secondary syphilitic eruption in relation to tattooed figures in the skin.

In the earliest reports attention was called only to an accentuation of the secondary eruption in and near the tattoo; in the later reports, for the most part, an accentuation of secondary papules in the blue portion of tattoo was emphasized, while the bright red portions ordinarily escaped. Since it was known that the bright red usually used was vermilion (mercuric sulphide) the conclusion was fairly obvious that the lack of eruption in the red portions was due to the protective quality of the mercuric ion.

The accentuation of papules in the other tattoo colors has been variously explained as due to irritation, and on the basis of the injected pigment causing areas of lowered resistance. In support of the theory of irritation as the cause, it is pointed out that papules of syphilis ordinarily are more profuse in the warm, moist areas which are apt to be the site of irritating discharges. This is particularly true in the region of the genitalia and perineum. However, it is also pointed out that cinnabar causes a much more severe local reaction immediately after injection than any of the other pigments, while in old tattoo the reaction is apparently equal, regardless of the type of pigment used.[2]

Not all observers have noted an absence of syphilitic papules from the red portions of tattoo which are said to be cinnabar, but it might also be pointed out that in no case in which such papules have been reported has the pigment been chemically proved to be cinnabar.

In the available literature I found only nine reports in which the authors state definitely that they were dealing with tattoo and secondary syphilis. To these might be added one of the cases reported by Maury and Dulles.[1] This case occurred in one of a group of fifteen patients

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* Studies and contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Maury and Dulles: Syphilis Communicated by Tattooing, Am. J. M. Sc. **75**:44, 1878.

2. Dohi: Tätowierung und Syphilis, Arch. f. Dermat. u. Syph. **96**:3, 1909.

infected by the same tattooer, and the authors definitely stated that some of the papules occurred in the red portion of the tattoo, and also that the pigment used was vermilion (mercuric sulphide). Further studies were not carried out.

Zechmeister [3] cites cases seen by Roma and Plummert in which a secondary syphilitic eruption was greatly accentuated in the tattooed area. The colors concerned in this accentuation are not mentioned and further studies were not done.

Wechselmann [4] reports a case in which the tattoo design was elevated above the surrounding skin and thrown into relief by the large number of papules occurring in this region. He cites a second case in which an attempt had been made to remove the tattooed design. A subsequent secondary syphilitic eruption became so accentuated around the remaining particles of pigment that the design was reproduced by the eruption. Apparently no further studies were made.

Lipschütz [5] reports a recurrent secondary syphilitic eruption sharply localized to a tattoo which did not occur anywhere else on the body.

Holland [6] reports four cases in three of which the localization of secondary papules in tattoo was not characteristic; but the fourth patient showed a much more striking predilection. He arrives at the conclusion that occurrence of secondary syphilitic papules in the blue portion of the tattoo is the rule, and occurrence in the red portion, the exception.

Florange [7] reports two cases in one of which there were secondary papules only in the blue portion of the tattoo while in the other they were present in the red, the blue portion being entirely free from them. Further work was not done.

Bernheim and Glück [8] cite an interesting case in which recurrent secondary papules appeared in a tattoo shortly after embellishment of an old tattoo with cinnabar. Further, this eruption appeared after some antisyphilitic therapy. Biopsy in this case showed "ulcerocrusted syphilis," but nothing further is said of the microscopic picture.

Keidel and Zimmermann [9] report a case in which the lesions of secondary syphilis were markedly accentuated along the tattoo lines, particularly in the blue and carmine red portions. They also state, however, that while they were few, papules also appeared in the

3. Zechmeister: Tätowierung und Syphilis, Monatschr. f. prakt. Dermat. **32**:225, 1901.

4. Wechselmann: Case Report, Dermat. Ztschr. **12**:557, 1905.

5. Lipschütz: Case Report, Arch. f. Dermat. u. Syph. **78**:381, 1905.

6. Holland: Beiträge zur Frage: Tätowierung und Syphilis, Arch. f. Dermat. u. Syph. **110**:393, 1911.

7. Florange: Beiträge zur Frage: Tätowierung und Syphilis, Dermat. Ztschr. **16**:783, 1909.

8. Bernheim and Glück: Beiträge zur Frage: Tätowierung und Syphilis, Dermat. Centralbl. **15**:162, 1911-1912.

9. Keidel and Zimmermann: Tattooing and Syphilis, Am. J. Syph. **2**:83, 1918.

cinnabar red. Plans to make a microscopic study in this case failed because of the patient's failure to return to the clinic.

Dohi [2] appears to have been the first to study extensively the question of altered distribution of secondary syphilis in tattoo. He found accentuation of lesions in the blue portion of the tattoo, but none in the red pigment used in his case. After chemical studies, he concluded that the red was cinnabar. In his article he enters into rather lengthy discussion of the reason for accentuation of lesions in the blue and their absence from the red.

Microscopically, he found the blue and red tattoo material in the upper portion of the corium, and both types largely intracellular. Most of these pigment containing cells were in the perivascular lymph spaces, and here also were found a few mononucleated round cells and spindle shaped cells. The epidermis was practically normal. The sections in which there were secondary papules showed an infiltration of round and spindle shaped cells so dense that the cells containing tattoo pigment were forced to the periphery. This infiltration penetrated deeply along the follicles and sweat glands and obliterated the papillae. He found no difference between the number of cells in the blue and red tattoo in sections in which syphilitic papules were not present.

Aoki [10] publishes an interesting account of his case, and, in the main, his observations are similar to those of Dohi.[2] However, he carried his work somewhat further and says that he succeeded in demonstrating *Spirochacta pallida* in his sections. Further, he carried out an experiment which is somewhat enlightening. Some weeks after tattooing red (cinnabar) and blue pigment into opposite sides of a rabbit's scrotum, he inoculated both areas with material containing large numbers of *S. pallida*. He reports that the result of this experiment was a chancre in the blue portion and none in the red, which indicates that cinnabar has some protective action against syphilis, even early, when its irritative effect is greater than that of the blue pigment.

Practically all of these observers point out a localizing effect of tattoo on secondary syphilis; some of the patients, indeed, showed an eruption only in the tattooed area. In addition, Maury and Dulles,[1] Florange,[7] Bernheim and Gluck [8] and Keidel and Zimmermann [9] definitely state that papules occurred in cinnabar red, while in one of the patients of Florange [7] and in the patient of Bernheim and Gluck [8] they occurred only in the red. However, it should again be pointed out that in none of these cases was the red pigment proved chemically to be cinnabar.

While the pathologic appearance of tattoo and secondary syphilis has been quite fully described by Dohi [2] and Aoki,[10] to the present

10. Aoki: Zur Frage: Tätowierung und Syphilis, Dermat. Ztschr. **19**:508, 1912.

time no photomicrographic material seems to have been published. This material is available in two of our cases, and for that reason I will add them to the existing reports.

REPORT OF CASES

CASE 1.—The patient presented on examination a generalized papular and papulosquamous syphilid and a residual induration in the prepuce. On both forearms there were tattoo designs done in dark blue, green and vermilion (mercuric

Fig. 1 (case 1).—Close-up of right forearm in case 1. The area within the diamond shapes in the tattooed bracelet is cinnabar red. Biopsy from radial edge.

sulphide). In all the designs papules were present in the green and blue, but apparently not in the red. This was made more apparent by the fact that here and there papules occurred in the blue outlining the red, but appeared to stop sharply when the red portion was reached. Since this eruption was extremely profuse, it is assumed to have been more than a mere coincidence that all the red was spared. In this case (fig. 1) the papules were not more numerous in the tattooed areas than elsewhere on the body. One of the papules which occurred in green and blue and appeared to stop sharply on the red side of the blue line was excised for microscopic examination. Its appearance will be described later.

Case 2.—The patient presented a generalized but sparse, papular and papulopustular syphilid, and a residual induration in the prepuce. He had several tattoo designs on the arms done in dark blue and two shades of red. The most interesting design (fig. 2) was that of a woman's head and shoulders; the outline, hair and upper portion of the chest were done in dark blue, the cheeks and petals of the floral design in typically vermilion red; and the region of the lower jaw and upper part of the neck in brownish red. In this case, the hair and upper portion of the chest of the tattooed figure presented clusters of papules as did the blue of the

Fig. 2 (case 2).—Tattooed figure from forearm, showing many papules in the blue and brownish-red but none in the cinnabar red which colored the cheek and petals of the floral emblem.

other designs. In no case did a papule or pustule appear in the vermilion, but in the brownish-red portion at the angle of the jaw of the tattooed figure, a pustule the size of a pea appeared and almost obliterated this portion of the tattoo. In this case there were distinctly more papules in the blue tattoo than on a corresponding area of skin anywhere else on the body. Papules from the blue part and the large pustule contained in the brownish-red area were excised for microscopic examination.

Both patients had had their tattoo designs for several years. One of them showed a distinct tendency toward localization of secondary

syphilis in the blue part of the tattoo, but neither showed a papule in that portion of the tattoo which was typically vermilion.

Microscopic Examination.—The specimen in figure 3 was taken from an old tattoo, half red and half blue, in otherwise apparently normal skin from the flexor surface of the forearm. It showed the tattoo material scattered throughout the upper and middle layers of the corium. This section was presented particularly to show the absence of infiltrate in the region of the tattoo pigment which might be interpreted as a foreign body reaction.

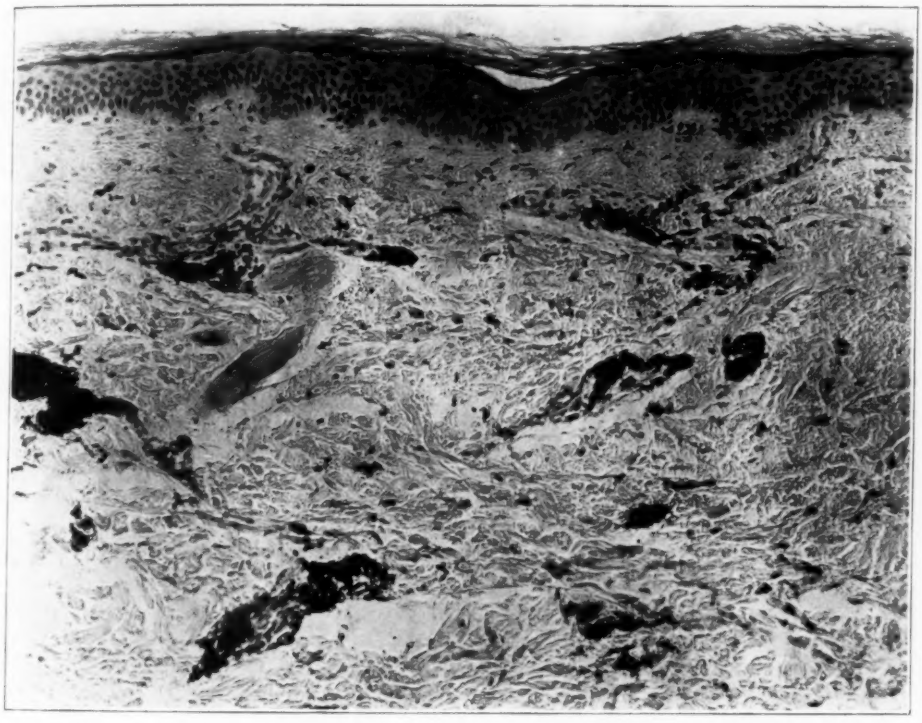

Fig. 3.—Section of tattooed but otherwise apparently normal skin, showing little infiltrate in the region of the foreign pigment.

Figure 4 shows a section taken from the forearm of patient 1. This papule before excision lay in the green and blue area and apparently stopped sharply at the red. It was cut in such a manner that three fourths contained green and blue while the other fourth contained red pigment.

The epidermis of the green and blue portion was mildly thickened and showed some parakeratosis and acanthosis, while the epidermis of the red portion was fairly normal. Both portions contained a few wandering cells in the prickle cell layer, but foreign pigment was not present.

The upper portion of the corium contained three types of foreign pigment in the form of granules of varying size. At one side, the pigment was bluish green and the granules were for the most part several times as large as a leukocyte. There were, however, many smaller granules of the same material which

appeared to be intracellular. At one point a large giant cell with peripherally arranged nuclei was seen containing a large granule of this pigment. The cellular infiltrate in this portion began in the papillary layer and extended deep down into the corium. It was composed largely of lymphocytes and plasma cells which showed a distinct predilection for the perivascular, periglandular and perifollicular spaces. The vessels of the corium were engorged, and here and there newly formed capillaries were found. Toward the center of the section a second type of pigment was present, the granules and clumps of which were only slightly smaller than those first mentioned. In bright light these granules were dark blue and black, and they remained so in subdued light. The infiltrate and vascular changes here were of the nature already noted, being, however, slightly less extensive.

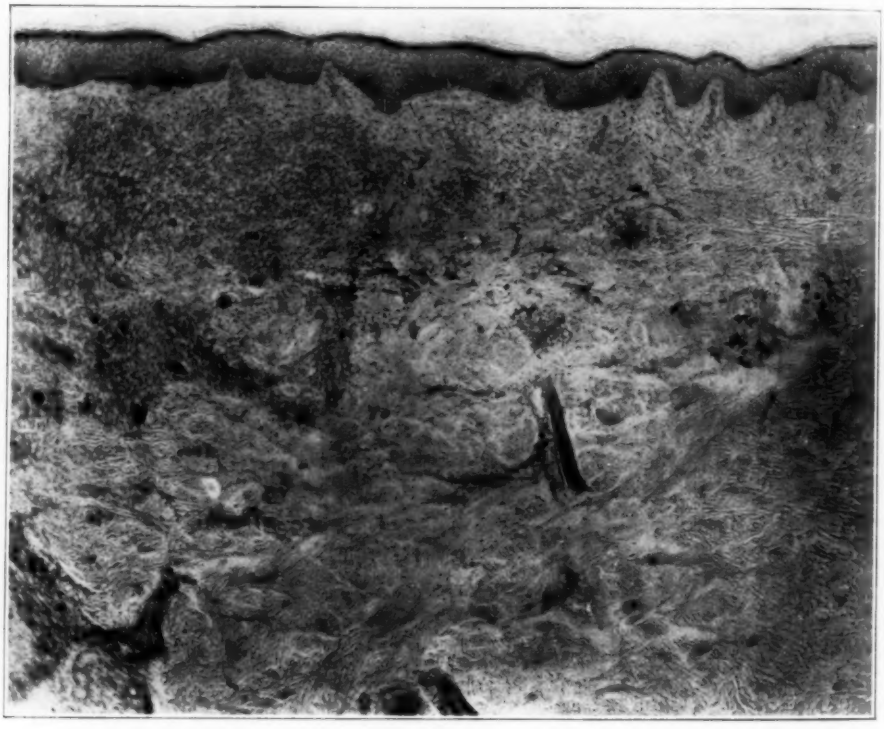

Fig. 4.—Marked syphilitic infiltrate in the region of the green and blue pigment and sharp disappearance of this infiltrate when the third type of pigment is reached.

At the opposite end of the section, there was a third type of pigment which consisted of smaller intracellular granules, many of which were arranged in clumps. In bright light, these granules were black, but in much subdued light, they became brownish red. In unstained sections they were dark brown and became in subdued light brilliant yellowish red. This is the microscopic appearance which was previously described for cinnabar in tattoos, and the chemical tests described by Dohi[2] showed that the dye was cinnabar. In continuing the examination from the middle area to this portion of the section one noted that the infiltrate which was so apparent in the two portions previously noted had rather

suddenly surprisingly decreased in the upper portion of the corium. This decrease in infiltrate corresponded fairly accurately to the distribution of the third type of pigment. The vessels in this region were still slightly engorged. Deep in the corium under the pigment which had been proved to be cinnabar, a fairly well marked perivascular and periglandular infiltrate of round cells such as were noted in the first two portions of the section was found.

Figure 6 shows a section taken in case 2. Before excision, this pustule lay at the angle of the jaw of the tattoo figure and was wholly in the brownish-red pigment. It stopped rather sharply at the cinnabar red in the cheek.

The epidermis had disappeared from the surface of the pustule and in the upper layers of the corium a fairly dense infiltrate consisting mostly of lymphocytes and plasma cells was found. These showed some predilection for the perivascular

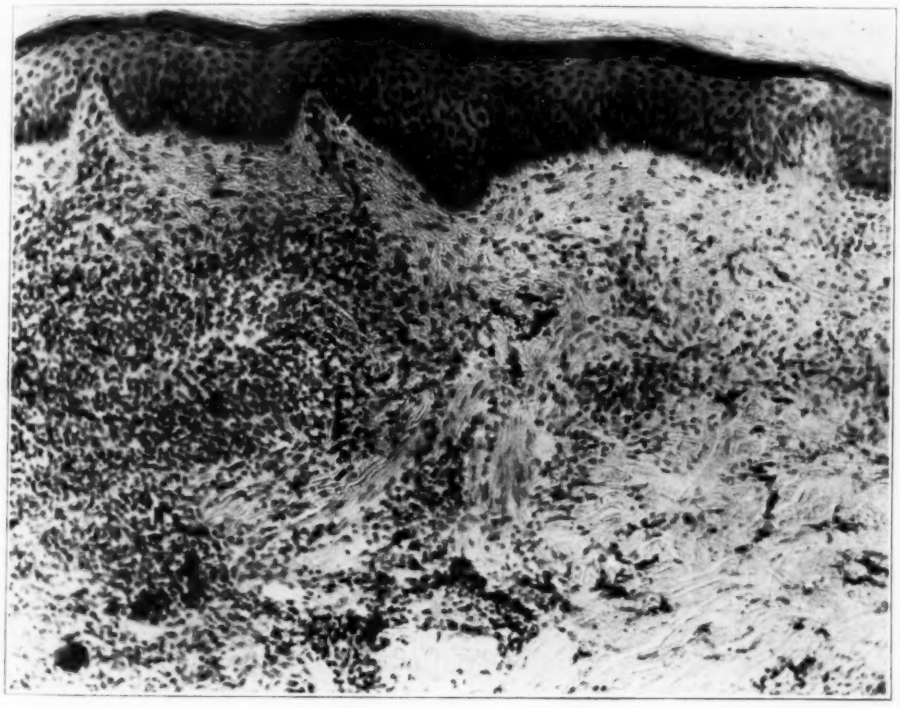

Fig. 5.—High-power magnification of figure 4 showing type of infiltrate and its sharp decrease as the cinnabar is reached.

spaces, and the vessels were greatly engorged. In this portion there was also a foreign dark brownish-red pigment, mostly intracellular, which was granular in appearance, and which did not respond to the tests for cinnabar.[2] The berlin blue reaction was positive for iron in this brownish-red pigment.

Toward the end of the section which showed the second type of pigment, the epidermis was fairly normal. The upper and middle portions of the corium showed foreign body pigment which responded to the tests for cinnabar. The infiltrate which was so marked in the portions already described had suddenly disappeared. This picture was approximately the same as that shown in figure 4. Spirochetes were not demonstrated in any sections, although repeated attempts were made in sections from both patients.

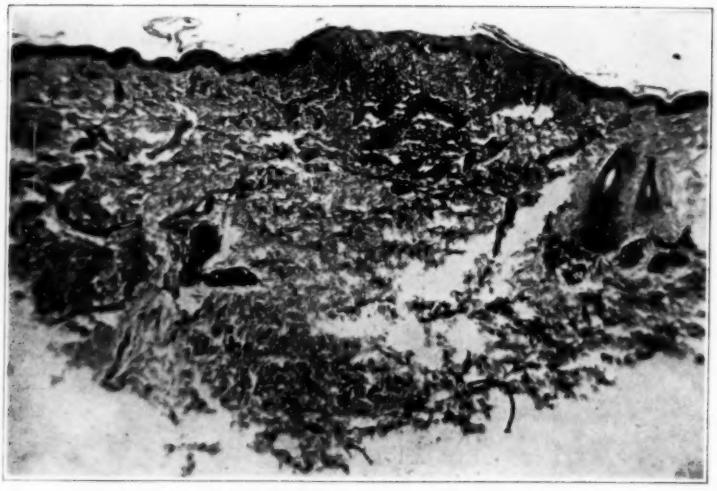

Fig. 6 (case 2).—Low-power magnification showing pustule from the angle of the jaw of the tattooed figure. Pustule was wholly in brownish-red pigment and stopped sharply at the cinnabar red.

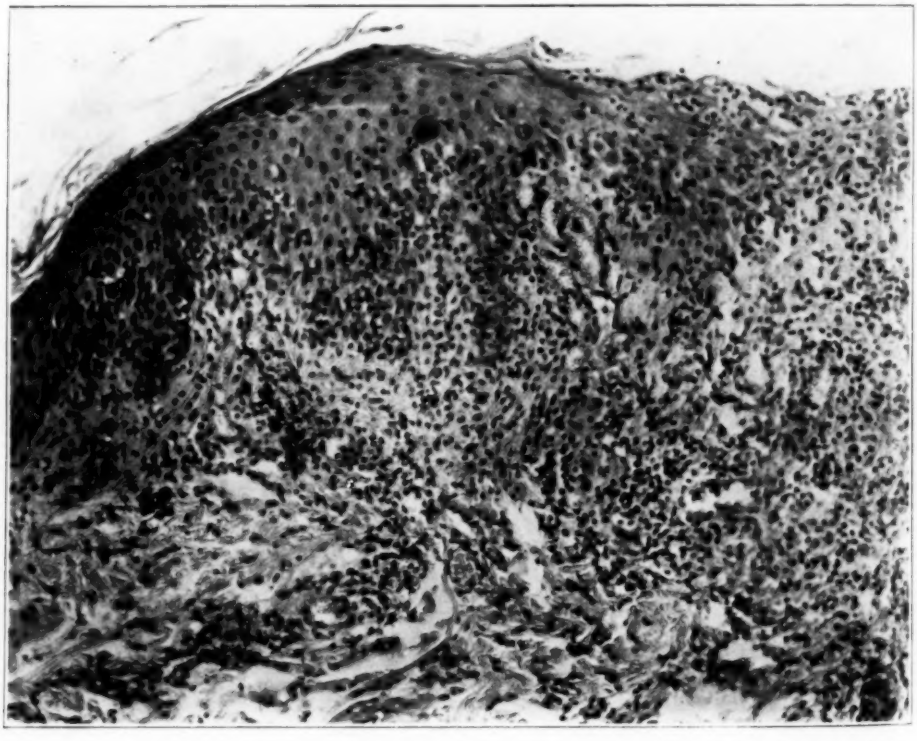

Fig. 7.—High-power magnification of figure 6, showing type of infiltrate and tattoo pigment.

COMMENT

From the literature previously published there can be little doubt that tattoo alters the distribution of secondary syphilis. Practically all observers have pointed out this fact and variously ascribed the cause of accentuation of lesions in the blue, green and so-called carmine red to irritation or to a lowered resistance in that area due to the foreign pigment. That it is due to an irritative effect of the tattoo material would seem unlikely, because sections of old tattoo show practically no infiltrate which certainly would be present as a foreign body reaction if such irritation were there. This is shown in figure 3, and has been repeatedly true in other biopsies. Dohi [2] also calls attention to this point. It would seem that an area of lowered resistance is produced by the presence of the foreign pigment which makes the site more favorable for the growth of spirochetes.

From this standpoint, it would seem that areas tattooed with cinnabar should also present a lowered resistance, and I have no doubt that they do. However, the protective influence of the mercuric ion must also be evaluated, and whether or not the secondary syphilitic eruption appears in cinnabar depends on the sum of these two opposed factors.

In neither case presented here did a papule appear in the cinnabar. This would seem to indicate that the protective influence of the mercuric ion was greater than the effect of the foreign pigment in lowering the resistance of the area. On this basis it is conceivable that in some instances the papules might appear in cinnabar; and this probably is the basis on which one must explain the four reports cited in this paper, that secondary syphilitic papules appeared in cinnabar tattoo. The other possibility lies in the fact that in these cases the material was not proved chemically to be cinnabar. Perhaps the authors were mistaken in the type of pigment used.

CONCLUSIONS

1. Two cases demonstrating the alteration of the eruption of secondary syphilis by tattoo are presented.

2. One case demonstrates the accentuation of the eruption in tattoo other than that done with cinnabar.

3. In neither case did a syphilitic papule appear in cinnabar area.

4. In no case in which secondary syphilitic papules have been reported in tattoo with cinnabar has the pigment been chemically proved to be cinnabar.

5. Whether or not the secondary syphilitic eruption appears in cinnabar tattoo depends on the sum of the opposed factors of lowered resistance and the protective influence of the mercuric ion. Usually this eruption will not appear in areas of cinnabar; occasionally it may.

LOCAL ACCIDENTS FOLLOWING THE INTRAMUSCULAR ADMINISTRATION OF SALTS OF THE HEAVY METALS

REPORT OF TWO CASES OF EMBOLIA CUTIS MEDICAMENTOSA *

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The intramuscular administration of the salts of heavy metals, as used in the treatment of patients with syphilis, has always been looked on as connected with certain risks as there have been a number of local accidents which could hardly be altogether eliminated. Of late, Barthélemy [1] has studied the accidents occurring after injections of the insoluble bismuth salts and has come to the conclusion that three factors may be responsible for them: the condition of the muscle tissue, the peculiar qualities of the drug and faulty technic. Barthélemy's [1] statement with special reference to the insoluble bismuth salts may really be applied with certain restrictions to heavy metal salts in general

In some patients, the drug is absorbed fairly well, but the muscle tissue becomes fibrous. The French speak of this condition as "fesses de bois." When an attempt is made later to give another injection in the same location, the needle meets considerable resistance, as if it were piercing an old scar.

Deep-seated infiltrations are seen sometimes after the first few injections of mercury or bismuth. Later, the injections become less painful and local reactions do not occur; or reactions cease after a short time, and one gains the impression that the tissues are absorbing the drug more readily. Occasionally, infiltrations may undergo suppuration and form sterile abscesses early after the patient has had considerable treatment, and it is difficult to say which one of the three possible factors is responsible. It may be stated, however, that the qualities of the drug are of great importance. After the administration of insoluble bismuth salts as bioleate, bisalicylate and potassium bitartrate, one sees fewer reactions of this type than are usually seen after injections of mercuric salicylate, mild mercuric chloride or mercurial oil.

After the injection of bismuth hydroxide, deep-seated cysts ("abcés aseptique profond Lortat-Jacob and Roberti,[2]" "enkystement grave"

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1. Barthélemy, R.: Accidents locaux des injections intramusculaires de produits bismuthiques insolubles en suspension huileuse, Ann. d. mal. vén. **20**:570 (Aug.) 1925.

2. Lortat-Jacob, L., and Roberti, J.: Abcès aseptiques profonds consécutifs aux injections d'hydroxyde de bismuth, Bull. Soc. franç. de dermat. et syph. **32**: 345, 1925.

Montlaur [3]) are observed rather frequently. These reactions begin slowly, at least one month after the injection, are inflammatory and cause a swelling of the entire buttock. There is no rise of temperature, no suppuration, and the cultures remain sterile. Picon [4] examined the mucinous sanguinolent fluid in the cysts, and found that the fatty acid of the vegetable oil is saponified through the action of the bismuth hydroxide. The end-product of this saponification is so voluminous that absorption is difficult. Other oily cysts are due to the chemical composition of the injected drug, but may also be found when the base is not absorbed as demonstrated by Binet [5] in experiments on animals.

The most common accident attributed to faulty technic is the formation of a node. These tumors are round, lobulated, hard, persistent and without inflammatory reaction or a tendency to be absorbed. They occur especially in adipose women when the depot of mercury or bismuth is set above the fascia. The medicine then flows back into the subcutis at the point of least resistance, where it is encapsulated through the condensation of the connective tissue. Occasionally, the nonabsorbed fluid may break through the skin.

It is a well known fact that injecting mercury or bismuth into or close to a major nerve may result in paralysis. Strictly aseptic technic easily prevents infection through the drug or the needle.

Another accident which is liable to happen, and for which faulty technic is blamed, is that the drug may be injected into a blood vessel.

When a soluble salt is accidentally injected into a vein, as a rule there are no ill effects, since the salt is diluted rapidly by the blood stream. The result may be more serious when the suspension of an insoluble salt finds its way into a vein. The cardinal symptom is a violent cough immediately afterward, sometimes accompanied by bloody sputum. Usually this condition clears up rapidly. Reports may also be found in the older and more recent literature (Magnus [6] and Chenoy [7]) in which it is stated that death occurred a few hours after the injection. Acute intoxication from the bismuth or mercury then occurs, with pulmonary embolism as the cause of death.

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3. Montlaur, H.: Un cas d'enkystement grave après injections intramusculaires d'hydroxyde de bismuth en suspension huileuse, Bull. Soc. franç. dermat. et syph. **32**:294, 1925.

4. Picon, M.: Sur la pureté et l'emploi de l'oxyde et du carbonate de bismuth, J. de pharm. et de chim. **3**: 58, 1926; abstr., Zentralbl. f. Haut-u. Geschlechtskr. **22**:435 (Feb. 20) 1927.

5. Binet, Léon: Recherches physiologiques sur la résorption de l'huile injectée sous la peau, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:1458 (Nov. 20) 1925.

6. Magnus: Ueber einen plötzlichen Todesfall nach intra-venöser Wismuteinspritzung, Klin. Wchnschr. **3**: 1275 (July 8) 1924.

7. Chenoy, C. F.: A Case of Death Due to Bismuth Injection, Indian M. Gaz. **61**:234, 1926.

HISTORY

The accidental injection of mercury or bismuth into an artery, of course, was always considered within the range of possibility, but there was no clear conception of what would happen in such a case until Walter Freudenthal's [8] report before the Schlesische Dermatologische Gesellschaft on Nov. 24, 1923. In Jadassohn's clinic, Freudenthal observed general malaise, reddening and swelling of the buttock with pain radiating into the leg following the intragluteal administration of bismuth subsalicylate. Around the site of injection there was a localized exanthem resembling somewhat livedo racemosa, with a tendency to necrosis in certain parts. On histologic examination of his last case, he found the cutaneous arteries blocked with the needle-shaped crystals of bismuth subsalicylate. From these observations, he drew the conclusion that the emulsion was injected into a deep artery, and that subsequently the cutaneous arteries were embolized by the crystals. In a recent publication, Freudenthal [9] advanced the theory that not only injection into an artery but also an injection into the arterial wall might cause accidents. This theory seems to be supported by the fact that in some instances blood was not obtained on aspiration, and that the characteristic pain was not experienced until from two to three hours after the injection. He expressed the belief that in these cases a bismuth depot was set close to the intima. The intima became necrotic, and then the drug reached the lumen of the blood vessel. This theory does not seem probable, since one can hardly assume that the intima might become necrotic within a few minutes or hours. Freudenthal's discovery explained a number of puzzling reactions seen after the injection of heavy metals salts; these have been reported in the literature by Touton,[10] Hildes,[11] Lesser,[12] Brocq,[13] Mayer,[14] Saphier,[15] Jad-

8. Freudenthal, Walter: Lokales embolisches Bismugenol Exanthem, Sitzungsbericht der Schlesischen Dermatologischen Gesellschaft vom 24 November, 1923; Zentralbl. f. Haut-u. Geschlechtskr. **11**:400 (April 5) 1924; Arch. f. Dermat. u. Syph. **147**:155, 1924.

9. Freudenthal, Walter: Medikamentöse Hautembolien (mit Exanthem, Blasenbildung, Gangrän): Embolia cutis medicamentosa (examthematica, bullosa, gangraenosa) (lokales embolisches Bismugenol-Exanthem), Arch. f. Dermat. u. Syph. **153**:730, 1927.

10. Touton, quoted by Freudenthal: Zoster femoralis nach Hg salicyl.-Injection, Arch. f. Dermat. u. Syph., 1889, p. 775; Arch. f. Dermat. u. Syph. **147**:155 (April) 1924.

11. Hildes, quoted by Freudenthal: Jahrbuch d. bosn.-herzegow, Landesspitals, Vienna, 1898.

12. Lesser: Verhandlung der Gesellschaft der Charité-Aerzte, Dec. 15, 1898; Berl. klin. Wchnschr. **36**:353 (April 17) 1899.

13. Brocq, M. L.: Eschare volumineuse de la fesse consécutive à une injection d'huile biiodurée, Ann. de dermat. et syph. **2**:347, 1901.

assohn,[16] Oppenheim [17] and Noble.[18] In studying the report of these authors, there is little doubt that the accidents described were due to arterial emboli.

Since Freudenthal first described the clinical picture of arterial embolism, numerous authors in various countries have recorded similar observations, and some of them have studied the reaction taking place after the intra-arterial administration of heavy metals salts in carefully conducted experiments with animals.

Nicolau,[19] in Bucharest, after the intramuscular injection of a proprietary bismuth iodide preparation and in two instances quinine bismuth iodide, reported seeing a diffuse painful swelling of the gluteus muscle and a bluish-red, netlike discoloration with subsequent necrosis in the central part. On histologic examination, he found some of the cutaneous arteries embolized by the drug. There was little inflammation. In the papillary layer, the arteries and veins were greatly dilated and their lumina filled with a homogenous mass of disintegrated red blood cells. The hemoglobin had diffused into the surrounding connective tissue, a fact which, in Nicolau's opinion, explains the purple color of the exanthem in the absence of extravasation of blood. The cells of the sebaceous glands were frequently destroyed and replaced by leukocytes in such a way that the sebaceous glands seemed to be transformed into pseudo-abscesses. Nicolau succeeded also in reproducing an analogous clinical and histologic picture by injecting insoluble bismuth and soluble mercury preparations into the arteries of rabbits' ears. The soluble salts produced an even more severe reaction through endarteritic thrombosis.

Koževnikov [20] injected mercury salts suspended in petrolatum or in watery solutions into the femoral artery of 103 rabbits and 6 dogs.

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14. Mayer, F., quoted by Freudenthal: Inaug. Diss., Berlin, 1919.

15. Saphier, Johann: Zosteriforme Hautnekrose nach intramuskulärer Einspritzung von Hydrargyrum succinimidatum, München. med. Wchnschr. **68**:394 (April 1) 1921; **68**:990 (Aug. 5) 1921.

16. Jadassohn, J.: Zosteriforme Hautnekrose nach intramuskulärer Einspritzung von Hydrargyrum succinimidatum, München. med. Wchnschr. **68**:852 (July 8) 1921.

17. Oppenheim, M.: Blitzfigurähnliche Hautveränderung im unmitelbaren Anschluss en eine intramuskuläre unlösliche Quecksilberinjection, Sitzungsbericht der Wiener Dermatologischen Gesellschaft vom 25 Oktober, 1923; Zentralbl. f. Haut-u. Geschlechtskr. **11**: 286 (March 20) 1924.

18. Noble, in discussion on Oppenheim (reference 17).

19. Nicolau, S.: Dermite livédoïde et gangréneuse de la fesse, consécutive aux injections intra-musculaires, dans la syphilis; à propos d'un cas d'embolie artérielle bismuthique, Ann. d. mal. vén. **20**:321 (May) 1925.

20. Koževnikov, P. V.: Ueber die Ursache der Gangrän nach Einspritzung von Quecksilberpräparaten, Venerologija u. Dermatologija, 1925, p. 72; abstr. Zentralbl. f. Haut-und Geschlechtskr. **18**:626 (Nov. 20) 1925.

His experiments confirmed the correctness of Nicolski's theory that emulsions of insoluble mercury salts administered intra-arterially always produce necrosis in the tissue supplied by this artery. Soluble mercury salts caused necrosis in 92 per cent of the cases but only when the reaction interfered with the circulation of the blood.

Olessov [21] observed three cases of gangrene of the gluteal muscle, one of which occurred after injection of mercuric chloride. The author's experiments on animals are instructive. He injected a 10 per cent oil emulsion of mercuric salicylate and a 1.5 per cent watery solution of mercuric chloride into the ventricle of curarized frogs. The drug is immediately carried by the blood stream through the arteria lingualis to the tongue, the circulation of which may be studied without difficulty in vivo under the microscope. Olessov found that as soon as a particle of the oil emulsion blocks an artery, necrosis takes place if anastomoses with adjacent arteries are not present. The mercuric chloride solution first corrodes the endothelium of the capillaries, which become obstructed. Thrombi are formed in the small arteries owing to the damage to the intima. Moreover, the tissue supplied by the arteries becomes gangrenous if collateral circulation is not established. Olessov likewise injected mercuric salicylate and mercuric chloride into the arteries of rabbits' ears, and on histologic examination, reached the same conclusions.

Other cases of arterial embolism were reported in Europe by Nagel,[22] Wolf,[23] Brack,[24] Tonian,[25] Stein,[26] Barthélemy,[27] Jeanselme [28]

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21. Olessov, I.: Aetiologie der Gangrän der Glutäen nach intramuskulären Injectionen bei Syphilis, Venerologija i dematologija, 1926, p. 610; abstr., Zentralbl. f. Haut-u. Geschlechtskr. **22**:438 (Feb. 20) 1927.

22. Nagel, V.: Lokales embolisches Bismugenol-Exanthem, Beitrage zum gleichnamigen Aufsatz von Freudenthal in Band 147, Arch. f. Dermat. u. Syph. **148**:42, 1924.

23. Wolf, Max: Lokale embolische Bismutschaedigung, Sitzungsbericht der Wiener Dermatologischen Gesellschaft vom 22 Januar, 1925; Zentralbl. f. Haut-u. Geschlechtskr. **17**:131 (June 20) 1925.

24. Brack, Wilhelm: Ueber arterielle Embolien der Haut und der unterliegenden Gewebe nach intra-muskulären Wismutinjectionen, Schweiz. med. Wchnschr. **55**:681 (July 23) 1925.

25. Tonian, B.: Zwei Faelle von Gangrän nach Einspritzung von Hydrargyrum salicylicum, Russk. vestnik dermatologii **4**:417, 1926.

26. Stein, Ludwig: Schwere Nekrose infolge Sublimat Injection, Liječnički vjesnik **47**:778, 1925; abstr., Zentralbl. f. Haut-u. Geschlechtskr. **19**:549 (April 15) 1926.

27. Barthélemy, R.: Embolie artérielle par injection intramusculaire de carbonate de bismuth, Bull. Soc. franç. de dermat. et syph. **33**:372, 1926.

28. Jeanselme, E.; Lévy, George; and Huet, Léon: Placard ecchymotique et phlycténulaire, consécutif à une injection intra-fessière de Curalues, Bull. Soc. franç. de dermat. et syph. **33**:96, 1926.

and his co-workers, Gougerot,[29] Nardi,[30] Liebner,[31] Audry,[32] Schreus [33] Lommen,[34] Sézary [35] and Sabouraud.[36] In this country, I [37] reported three cases after the administration of potassium bismuth tartrate; in two of them, the first violent symptoms subsided within from two to three weeks; in the third case, an extensive necrosis of the skin of the buttock was accompanied by a peroneal paralysis. The slough in the buttock healed slowly, and the paralysis disappeared almost entirely, but five or six months after the unfortunate injection, the patient developed several trophic ulcers on the first, second and third toe. The patient is still incapacitated after a period of twenty months.

DIAGNOSIS

Arterial embolism, or "embolia cutis medicamentosa," as Freudenthal recently called the condition, is an entity which may be rather easily diagnosed clinically. Immediately or shortly after the supposed intramuscular injection of the insoluble mercury or bismuth salt, the patient complains of a violent pain radiating into the leg. There is a diffuse swelling of the gluteus muscle, with a bluish-red, marmoraceous, net-like discoloration of the skin near or around the site of injection. In some instances, especially after injections of mercury, certain parts of the discolored skin may become necrotic. After intra-arterial injection of soluble preparations, the clinical picture is essentially the same. In this instance, however, the obstruction of the blood vessels is due to an endarteritic thrombosis, as demonstrated by several investigators mentioned in this paper.

29. Gougerot, M., in discussion on Jeanselme, E.; Lévy, George; and Huet, Léon: Bull. Soc. franç. de dermat. et syph. **33**:96, 1926.

30. Nardi, Giona: Le emorragie interstiziali: Raro accidente in seguito alle iniesioni endomuscolari, Dermosifilografo **1**:173, 1926; abstr., Zentralbl. f. Haut-u. Geschlechtskr. **21**:900 (Jan. 5) 1927.

31. Liebner, Ernst: Hautgangrän nach Wismutinjektion, Dermatologische Zusammenkünfte, Sitzg. v. 1. 4. 1926, Zentralbl. f. Haut-u. Geschlechtskr. **21**:403 (Nov. 20) 1926.

32. Audry, C.: abstr. of Freudenthal's original article, Ann. de dermat. et syph. **6**:474, 1925.

33. Schreus, H. T.: Blitzfigurenartiges Exanthem nach Mesurol (Bi-Präparat), Dermat. Ztschr. **43**:69, 1925.

34. Lommen, A.: Bemerkungen zu der Arbeit "Schwere Nekrose nach Hg Cl_2 Injektion," Dermat. Wchnschr. **85**:1090 (July 30) 1927.

35. Sézary, M. A.: Embolie artérielle de la fesse consécutive à une injection intramusculaire d'hydroxyde de bismuth, Bull. Soc. franç. de. dermat. et syph. **33**:488, 1926.

36. Sabouraud, R.: in discussion on Sézary, M. A.: Bull. Soc. franç de dermat. et syph. **33**:488, 1926.

37. Gammel, John A.: Arterial Embolism: An Unusual Complication Following the Intramuscular Administration of Bismuth, J. A. M. A. **88**:998 (March 26) 1927.

Recently, I observed two more cases of arterial embolism, and the clinical picture in one of them was in more than one way different from my previous experiences and from the descriptions in the literature. Therefore I feel justified in reporting this case.

REPORT OF A CASE

A woman, aged 39, who had been under antisyphilitic treatment for a considerable time, on Feb. 1, 1927, received 1 cc. of 10 per cent potassium bismuth tartrate in vegetable oil. The injection, which was given by a medical student, was made into the lower inner quadrant near the center of the buttock. About one minute later, she complained of an excruciating pain in the right buttock, the right side of the genitalia and the region of the right side of the bladder. She was on the verge of collapse, and stimulants had to be given hypodermically. Respiratory difficulties, cyanosis or coughing were not observed.

The pain did not subside, and Dr. H. N. Cole, who saw the patient immediately afterward, suspected arterial embolism, so the patient was transferred to the hospital. Here, one hour after the injection, an area about 5 by 7 cm. was seen on the right buttock, which was pale and cold. It was surrounded by an irregular zone of hyperemia about 2 inches (5.08 cm.) wide. The tissues were barely infiltrated and not very tender on palpation. In addition to the pain, the patient complained of numbness in the genitalia, the region of the bladder, and the right buttock and a pain radiating into the right leg.

The next day the temperature rose to 39.2 C. (102.5 F.). The palm-sized area which had been pale the day before was now reddish blue, somewhat mottled and surrounded by an area of hyperemia. One bluish-red streak of about 1.27 cm. in width radiated toward the rectum, another one located to the inside of the buttock radiated upward into the right labium maius and minus. The right wall of the vagina was deep blue and discharged a serosanguineous fluid. Abduction of the foot and dorsal flexion of the foot or the toes was impossible—a typical peroneal paralysis. An ankylosis of the knee joint had been present since the patient was 24 years of age. Since the pain in the regions involved was still severe, a reliable examination for sensory disturbances could not be carried out. Urination and defecation were likewise painful. A catheterized specimen of urine showed numerous red and a few white cells. The white blood count was 20,000. The differential count showed polymorphonuclear leukocytes, 81 per cent; small lymphocytes, 6 per cent; large lymphocytes, 4 per cent, and transitionals, 9 per cent.

The third day the temperature rose to 40 C. (104 F.), but dropped gradually the following days until it reached the normal level on the twelfth day.

During the first three days, the pain was constant and most severe; then it disappeared and became manifest only on urination, defecation and active or passive movement. The right buttock showed only a moderate swelling and slight tenderness to palpation. The dark blue, mottled lesion remained cold; on the sixth day, soft bullae were noted in its center. When these were broken open, a serosanguineous fluid discharged and left a necrotic ulcer. Four days after the onset, I removed a small piece of skin and subcutaneous tissue from the upper portion of the bluish, disclored lesion on the buttock. When the incision was made, only a few drops of sanguinolent serum were oozing out, but no blood. On microscopic examination of the specimen, I found the capillaries maximally dilated and brown crystals of potassium bismuth tartrate that had been used for the injection in some of the small subcutaneous arteries. As soon as it was evident

to what extent the skin of the buttock would slough out, it was excised surgically in order to speed up the process of healing.

Cystoscopic Examination.—Dr. Louis G. Hermann performed the cystoscopic examination on Feb. 8, 1927. The urethral orifice appeared normal. A no. 21 cystoscope was introduced without difficulty and without pain to the patient. About 200 cc. of urine was obtained. The mucosa of the bladder did not show any pathologic changes. The trigonum was definitely injected. Both ureteral orifices were normal. On the right lateral wall just at the neck of the bladder, a definite slough could be seen. This lesion occupied about one third of the neck. It was attached, grayish-white, and sharply demarcated. The right lateral wall of the bladder was not involved in the process. The specimen of urine contained

Fig. 1.—The site of injection twenty-four hours afterward. The right buttock is swollen and shows a reddish-blue, roughly triangular, mottled area surrounded by a zone of hyperemia.

a few white blood cells and a few red blood cells, but otherwise was normal. The urethra was examined with the urethroscope and found to be normal throughout. The diagnosis was necrosis of the mucous membrane at the neck of the bladder on the right and acute trigonitis.

Microscopic examination.—On March 8, the urine from the bladder showed a few red blood cells, probably due to trauma, but white blood cells or casts were not noted. The mucosa of the bladder appeared normal except for a slightly more reddened area at the site of the previously existing slough. The entire neck of the bladder was examined thoroughly, but ulceration or sloughing could not be demonstrated.

Vaginal and Rectal Examination.—When the gangrenous lesion over the right buttock was excised by Dr. Simon A. Schlueter on February 12, a vaginal and

rectal examination was also performed under general anesthesia. An area of superficial necrosis of the mucous membrane extended along the wall of the vagina up to the level of the cervix. Proctoscopic examination revealed a similar ulceration about 2 cm. in diameter on the right lateral wall of the rectum just above the sphincter ani.

Neurologic Observations.—After the most severe pain of the first few days subsided, the patient complained of a painful pricking sensation in the lateral part of the lower limb, the dorsum of the foot and to a lesser degree on the planta pedis. The leg felt cold all the time. Perception of pain and light touch were absent over a triangular area over the dorsal surface of the right foot. All muscles supplied by the peroneal nerve were paralyzed. The response to galvanic and faradic current was slow, the peroneal muscles being most affected.

Fig. 2.—Small arteries and capillaries dilated, moderate degree of cellular infiltration.

Progress.—The proctoscopic and vaginal examinations repeated six weeks after the onset showed all ulcerations healed, and only a slight hyperemia marked the places where they had been. The wound on the buttock healed over by granulation within seven weeks. The improvement in the peroneal paralysis, however, was slow in spite of application of faradic and galvanic current, massage, heat and strychnine sulphate, 1 mg. three times a day. Walking was facilitated by a brace in the shoe. Now, after thirteen months, the patient is able to extend the toes dorsally just a little, and the zone of anesthesia on the dorsum pedis is narrower than in the beginning.

Histology.—The pathologic report was made by Dr. Paul T. Southgate, assistant resident pathologist, and his observations follow.

The sections of tissue taken five days after the injection of potassium bismuth tartrate presented the picture of a moderately severe dermal and subcutaneous inflammatory process. The capillaries were hyperemic. There was an infiltration of the tissue with an exudate consisting mostly of polymorphonuclear leukocytes and, to a lesser extent, of lymphocytes, endothelial cells and serous fluid.

Masses of dark brown crystalline substance which, in some instances, filled as much as two thirds of the lumina, were present in many of the subcutaneous vessels. Serial sections showed the same phenomena. A light brown, finely granular, amorphous material was also seen within the vessels in serial sections. This material, however, was for the most part within the endothelial cells lining the capillaries. In some areas, there were a few granules in the tissue and around the capillaries; these were morphologically similar to those within the endothelial cells of the capillaries. Granules were not seen in the area of most marked reaction. A suspension of potassium bismuth tartrate examined microscopically was found to be made up of dark brown crystals and light brown granules, morphologically identical with those seen in these sections. The crystals and amorphous granules in the tissue did not react to potassium ferrocyanide and

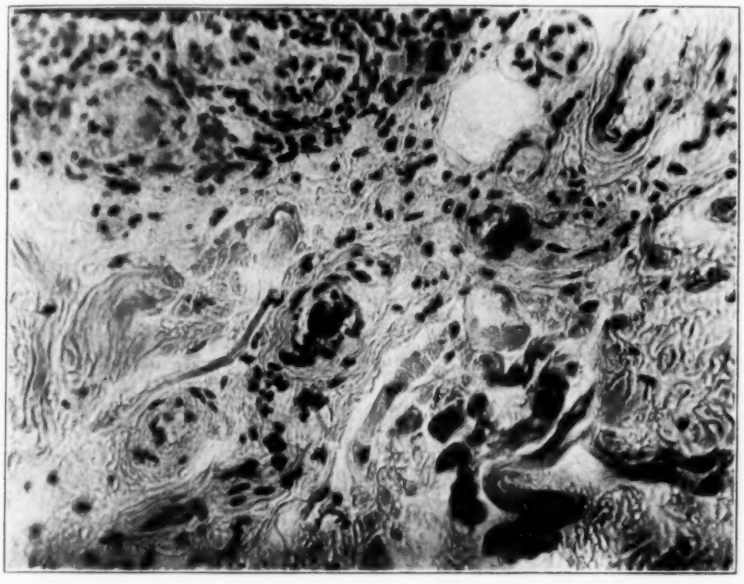

Fig. 3.—Two small arteries with bismuth crystals.

hydrochloric acid as does hemosiderin. The cellular infiltration was greatest in certain areas of areolar tissue found in the subcutaneous layer, containing capillaries, adipose tissue and coil glands. The epidermis, sebaceous glands, and the hair follicles did not show any pathologic changes in the sections taken five days after the injection. The red blood cells filling the capillaries were pale staining.

The sections of tissue taken twelve days after injection showed a similar, but much more severe, process. The cellular infiltration throughout the subcutaneous layer especially was much more marked. The cell types were proportionately the same as in the first sections. There was, in addition, a necrosis of the epidermis and the corium, involving also the cutaneous appendages. The subcutaneous tissue presented less destruction. Here, the necrosis involved only an occasional strand of connective tissue and the appendages. In many instances, the sebaceous glands and the coil glands were necrotic and infiltrated with polymorphonuclear leukocytes. The walls of the capillaries and small vessels were necrotic. One vessel was found to contain large crystals as compared with many vessels in the earlier sections. The granules had disappeared.

Fig. 4.—Subcutaneous artery partially filled with bismuth crystals.

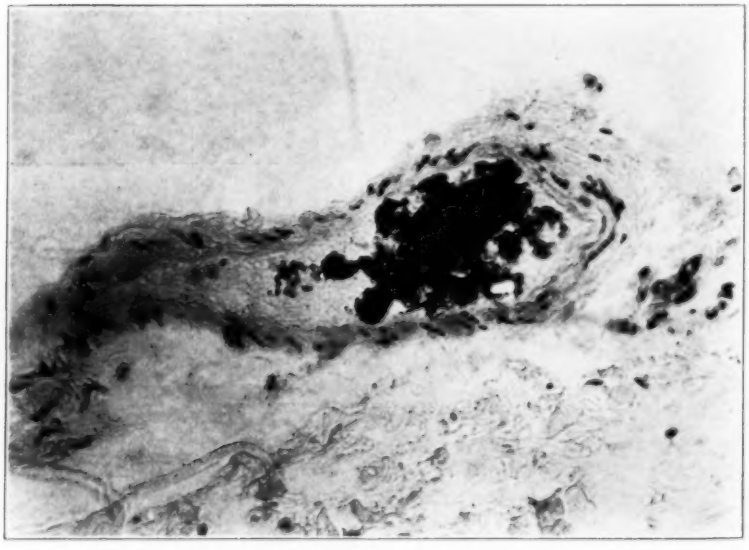

Fig. 5.—Same artery as in figure 4.

Nicolau, in describing sections of cutaneous and subcutaneous tissues following injection with a proprietary bismuth iodide preparation iodobismuthol, noted a marked destruction of the sebaceous glands with early abscess formation and a destruction of the red blood cells in the vessels. He also noted a diffusion of extracellular hemoglobin in the tissues. The sections at hand showed a similar destruction of the sebaceous glands in those taken twelve days after injection, but destruction was not noted in those taken five days after injection. The red blood cells in the five day sections were uniformly pale-staining, but not disintegrated. In the eighteen-day sections, the deeper vessels were, in several instances, thrombosed, and filled with disintegrated red blood cells. The more superficial vessels were empty or filled with cells, some of which were fragmented. A superficial area was present containing extracellular hemoglobin in the tissue, but from the distribution, this appeared to be due to hemorrhage occurring at operation.

Summary.—1. The sections taken five days after the injection of potassium bismuth tartrate showed the crystals and granules within the vessels, and a marked infiltration of the tissues with polymorphonuclear leukocytes, lymphocytes, endothelial cells and edema.

2. The sections taken twelve days after the injection showed considerably fewer crystals in the vessels and no granules. There was a much more marked cellular infiltration, with necrosis of the epidermis, corium and an occasional strand of connective tissue in the subcutaneous layer. The cutaneous appendages were necrotic. Some of the deeper subcutaneous vessels were thrombosed, with a destruction of red blood cells.

COMMENT

To my knowledge, this is the first time in the United States that crystals were demonstrated within arterial blood vessels following the administration of heavy metals salts as used in the treatment of patients with syphilis. Previous experiences with similar reactions enabled me to make a clinical diagnosis of arterial embolism a few minutes after the injection and to confirm it later by biopsy. The severe pain in the region of the bladder, the red and white blood cells in the urine, the discoloration of the vulva and the serosanguineous discharge from the vagina, as well as pain on defecation and bloody stools, led me to suspect a similar reaction in the bladder, vagina and rectum as well as on a circumscribed area on the buttock.

The drug apparently was injected into the arteria glutea inferior dextra or one of its major branches. This artery (Robinson [38]) has anastomoses with the arteria pudenda interna, branches of which go to the vagina and the rectum (rami posteriores labiales and arteria hemorrhoidalis inferior). The arteria pudenda interna again anastomoses with the vesical arteries. This rich net of anastomosis explains the extraordinary distribution of the lesions.

Most striking and unique in the literature is the fact that two of the four cases of arterial embolism were complicated by a peroneal paralysis.

38. Robinson, Arthur, in Cunningham's Text Book of Anatomy, New York, William Wood and Company, 1923, p. 942.

In the first paper on this subject, I ventured the opinion that a few bismuth crystals also reached the nervus peronaeus through the arteria comitans nervi ischiadici. The arteria glutea inferior and the nervus ischiadicus, of course, run in that particular location so close together that it was probable that the bismuth depot was set near to the nerve and that only a small part of the drug was injected into the artery.

I had the opportunity to observe a fifth case of arterial embolism in November, 1927. Immediately after the injection of potassium bismuth tartrate, the patient experienced a severe pain in the buttock; the pain then traveled down the leg. Two days later, he entered the hospital. On admission, the right buttock was swollen and tender. In the right upper outer quadrant, there was considerable induration over an area 4 by 7 cm., and the skin showed a bluish mottling. Pain, swelling and discoloration disappeared during the course of the following week, and the patient was discharged as well on the ninth day after the injection. A biopsy from the discolored portion of the skin showed considerable degeneration of the cells of the stratum granulosum and a slight lymphocytic infiltration of the corium. In one section, a small artery was seen completely plugged by a mass of dark brown bismuth crystals.

CONCLUSIONS

Accidents, such as those under discussion, are fortunately rare, these five cases being distributed over a series of about 45,000 intramuscular injections. What precautions can be taken to avoid them?

The place of injection is of greatest importance: intramuscular injections of mercury or bismuth should be given only into the upper and outer quadrant of the buttock. This is where the medical student who gave the injection in the fourth case reported made his mistake.

When aqueous solutions are injected intramuscularly, it may be sufficient to aspirate only in order to assure that the lumen of the needle is not within a blood vessel.

This safeguard is not sufficient when tenacious, creamlike suspensions are injected through a thin needle. Then it is probable that the viscosity of the drug prevents the backflow, especially when the needle does not fit the syringe perfectly. The importance of this point is clearly demonstrated by the fact that it is frequently impossible to draw mercuric salicylate or bismuth suspensions into the syringe through a fairly thin needle.

In this case, after assuring oneself that the lumen is not clogged up, the needle should first be inserted separately; after an interval of at least fifteen seconds the syringe should be attached, and after aspiration the injection completed.

Another method, used by many syphilologists, is to insert the needle, which is first attached to a syringe filled with sterile saline, aspirate, disconnect the syringe and needle, attach the syringe with the drug, aspirate again and then finish the injection.

One rather safe way which is found especially convenient in large clinics in which a great number of injections must be given in a limited time is to use a needle large enough to allow a good back flow. The more tenacious the suspension the larger the needle should be. A needle may be regarded as safe when it is possible to fill the syringe through the needle without any difficulties. It is true that small needles cause less pain than large ones, but this is of minor importance when one considers the greater chances taken with a small needle.

In spite of all these precautions, there still exists a possibility that after aspiration either patients or physician through an involuntary and unobserved movement pushes the needle in or pulls it out long enough to bring its lumen into a blood vessel. Unintentional intra-arterial or intravenous injections will occur now and then, but careful technic may reduce them to a negligible minimum.

LESIONS OF THE MUCOUS MEMBRANES IN EPIDERMOLYSIS BULLOSA

REPORT OF A CASE *

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Cases of epidemolysis bullosa were probably first described in 1879 by Tilbury Fox,[1] although Goldscheider [2] is credited with the first accurate description of the disease in 1882. It was not until 1886, however, that Köbner [3] gave the disease its present name and differentiated it from pemphigus and other bullous diseases.

Various observers have from time to time suggested other names for the condition. As a result of his examination of the sections, Goldscheider suggested the name "acantholysis bullosa." Payne's [4] case in 1884 was entitled "A Traumatic Bullous Affection Resembling Pemphigus." In 1897, Beatty [5] also classified the disease clinically with pemphigus under Payne's title. In 1898, Bowen [6] suggested the name "congenital bullous dermatitis" as being less prejudicial to the etiology. The French describe the disease as "congenital pemphigus." The term epidermolysis bullosa, however, as first suggested by Köbner, has been accepted by most dermatologists.

Since Tilbury Fox's paper in the London *Lancet* in 1879, over 300 cases of the disease have been reported in the literature. The disease is characterized by a marked hereditary nature, and men seem to be affected more often than women. Although some of the cases in adults appear to be acquired, Wise and Lautman [7] showed that others are closely allied to pemphigus, so that the question of the acquired type is not entirely settled as yet.

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1. Fox, Tilbury: Notes on Usual or Rare Forms of Skin Diseases: IV. Congenital Ulceration of the Skin (Two Cases) with Pemphigus Eruption and Arrest of Development Generally, Lancet **1**:766, 1879.

2. Goldscheider, A.: Hereditäre Neigung zur Blasenbildung, Monatschr. f. prakt. Dermat. **1**:163 (Aug.) 1882.

3. Köbner, H.: Hereditäre Anlage zur Blasenbildung, Deutsche med. Wchnschr. **12**:21, 1886.

4. Payne, H.: St. Thomas Hospital Reports, **14**:225, 1884.

5. Beatty, Wallace: Epidermolysis Bullosa, Brit. J. Dermat. **9**:301 (Aug.) 1897.

6. Bowen, J. T.: Congenital Bullous Dermatitis with Epidermic Cysts, J. Cutan. Dis. **16**:253 (June) 1898.

7. Wise, F., and Lautman, M. F.: Epidermolysis Bullosa Beginning in Adult Life: The Acquired Form of the Disease, J. Cutan. Dis. **33**:441, 1915.

The lesions of the mucous membrane in epidermolysis bullosa are inadequately described in the standard dermatologic textbooks. Zinsser's textbook on "Diseases of the Mouth," Butlin and Spencer's "Diseases of the Tongue" and FitzWilliam's "The Tongue and Its Diseases" do not make any reference to the disease.

A survey of 37 cases reported in the literature in which the mucous membranes were involved revealed that the oral mucosa was affected in 27, the throat and the pharynx in 3, the esophagus in 2, the eye in 3, the anus in 2, the penis in 4 and the intestine in 1. Involvement of the nasal and vaginal mucosae is not mentioned by any of the writers. In 16 of the 27 cases in which the oral mucous membrane was affected, the tongue was involved; in 15 cases the buccal mucosa was affected, in 7 the lips, in 6 the gums and in 5 the palate. In all of the cases studied there were associated cutaneous lesions.

SITES AFFECTED

The Tongue.—The mucosa of the tongue was more frequently involved than any of the other mucous membranes, bullae being the commonest lesions. Erosions from ruptured bullae were the next commonest lesions. In the cases described by C. Fox,[8] T. Fox,[1] and Kanoky and Sutton [9] the tongue was bound down by scar tissue resulting from the healing of old lesions. In Lapowski's [10] case there were fine vesicles on the tongue; in Engman and Mook 's [11] cases, small telangiectatic lesions, and in Wende's [12] case there were milk-white spots on the edges of the tongue. In Steuer's [13] case, the tongue was abnormally thick; while in Kaftan's [14] case, it was atrophied.

Klausner's [15] interesting case occurred in a young woman, aged 25. Because of bullae on the mucous membrane of the tongue and mouth,

8. Fox, Colcott: Epidermolysis Bullosa, Brit. J. Dermat. **17**:223, 1905.

9. Kanoky, J. P., and Sutton, R. S.: Epidermolysis Bullosa Congenita, J. A. M. A. **44**:1137 (April 12) 1910.

10. Lapowski, H.: Epidermolysis Bullosa, Arch. Dermat. & Syph. **5**:415 (March) 1922.

11. Engman, M. F., and Mook, W. H.: A Study of Some Cases of Epidermolysis Bullosa with Remarks upon the Congenital Absence of Elastic Tissue, J. Cutan. Dis. **24**:54, 1906.

12. Wende, G. W.: Epidermolysis Bullosa Hereditaria, J. Cutan. Dis. **20**:537, 1902.

13. Steuer, O.: Ueber Beteiligung der Schleimhaut des Mundes und der Speiseröhe bei Epidermolysis Bullosa Hereditaria, Arch. f. Ohren-, Nasen-, u. Kehlkopfh. **107-8**:11, 1921.

14. Kaftan, F.: Ein Fall der Epidermolysis Bullosa Hereditaria mit typischen Erscheinungen im Munde und an den Zahnen, Deutsche monatschr. f. Zahnheilkunde. **43**:165 (April) 1925.

15. Klausner, E.: Zugenkrebs als Folgezustand bei einem Falle von Epidermolysis Bullosa, Arch. f. Dermat. u. Syph. **116**:71, 1913.

the patient had severe pain when eating or speaking. She could not protrude her tongue beyond the line of the teeth. On examination the patient presented a painless swelling of the tongue with enlargement of the cervical glands. Biopsy showed squamous cell carcinoma. This is the only case reported in which a malignant condition developed on the site of old lesions.

The Buccal Mucosa.—The buccal mucosa, next to the tongue, was the mucous membrane most commonly involved. Bullae were the commonest lesions. In Vyosky's [16] case, ecchymoses were present; in Rosen's,[17] superficial erosions, and in one of Wise and Lautman's [7] cases, pea-sized, yellow vesicles. Blumer [18] ascribed the development of bullae in his case to the absence of teeth in his patient and the consequent irritation from the unmasticated food.

The Lips.—Bullae were present in Pernet's [19] and in MacKee's [20] cases, while in one of Engman and Mook's [11] cases epidermic or milia-like cysts were noted. Thin cicatrices were mentioned by Engman and Mook and by C. Fox [8]; ecchymoses, by Vyosky.[16] Schamberg's [21] case was that of a negro who presented a leukokeratosis.

The Gums.—In Sibley's [22] case, bullae were present. Vyosky [16] mentioned gingivitis, T. Fox [1] white patches, and Wise and Lautman [7] erosions. Kaftan [14] suggested that the bullae in the case reported by him were caused by irregular teeth. Following the extraction of one of the teeth, a bulla appeared at the site of the needle puncture.

The Palate.—In Vyosky's [16] and Kaftan's [14] cases, bullae were present on the soft palate. Wise and Lautman [7] and Lapowski [10] mentioned fine yellowish vesicles on the hard palate. In Pautrier's [23] case, there were bullae with hemorrhagic contents on the palate.

Throat and Pharynx.—In Morris' [24] and Kaftan's cases there was a history of bullae in the throat. In one of T. Fox's [1] cases, "the throat

16. Vyosky, Y.: Epidermolysis Bullosa Hemorrhagica, Céska Dermat. **3**:16, 1922.

17. Rosen, I.: Epidermolysis Bullosa, abstr., Arch. Dermat. & Syph. **7**:275 (Feb.) 1923.

18. Blumer, C.: Hereditäre Neigung zu traumatischer Blasenbildung, Arch. f. Dermat. u. Syph. **2**:105, 1892.

19. Pernet, G.: Epidermolysis Bullosa (Congenital Pemphigus), Brit. J. Dermat. **16**:225, 1904.

20. MacKee, G. M.: Epidermolysis Bullosa Hereditaria, abstr., Arch. Dermat. & Syph. **13**:709 (May) 1926.

21. Schamberg, J. F.: Epidermolysis Bullosa, abstr., Arch. Dermat. & Syph. **5**:678 (May) 1922.

22. Sibley, W. K.: Case of Epidermolysis Bullosa, Brit. J. Dermat. **27**:190, 1915.

23. Pautrier, L. M.: Pemphigus congénital, à kystes épidermiques, Bull. Soc. franç. de dermat. et syph., May 8, 1921.

24. Morris, Malcolm: Epidermolysis Bullosa, Brit. J. Dermat. **14**:171, 1902.

upon examination, was found sore and ulcerated, the tongue blistered and reddened, and bullae which had appeared the night before had left a slight ulceration."

The Esophagus.—Morris [24] alluded to a case in his practice in which large casts of the esophagus were occasionally brought up. Steuer [13] described an interesting case in a man, aged 29, who entered his clinic for treatment for a supposed foreign body in the throat. Four or five days after an esophagoscopy had been performed, typical lesions appeared in the upper third of the esophagus and at the esophageal orifice. There were numerous bean and cherry-sized bullae, some containing reddish fluid, and several erosions of various sizes covered with a fibrinous exudate.

The Penis.—In Wende's [12] striking case there were erythematous lesions about the meatus. The patients in the cases described by Colombini [25] and Bonaiuto [26] developed bullae on the glans and prepuce following intercourse. In one of Wise and Lautman's [7] acquired cases, there was one large bulla on the glans.

The Eye.—The eye is rarely involved in epidermolysis bullosa, the changes usually being secondary to the cutaneous lesions. In the primary cases, the possibility of pemphigus must be considered, especially in adult cases. In Wende's [12] case, there was a blepharitis and an associated conjunctivitis. In C. Fox's [8] case, there was shrinking of the conjunctivae, while Pernet [19] describes a haziness of the periphery of both corneas with some dilatation of the peripheral blood vessels.

The Intestine.—In Kaftan's [14] case, there were intestinal disturbances. There was a history of painful defecation, and examination of the stool showed blood and shreds of mucous membrane.

The Anus.—Involvement of the anus occurs infrequently. Wende [12] and Wise and Lautman [7] mentioned bullae in this region in their cases.

REPORT OF A CASE

History.—H. P., a boy, aged 9, was first seen at St. Mary's Dispensary in May, 1925. At that time, he had a generalized bullous eruption and several areas of pigmentation on the trunk.

A brother of the patient was said to have had a similar condition, but he had died in early infancy. There was no history of the disease in the parents or their relatives.

Delivery occurred at full term and was normal. About one-half hour after birth, bullae were noticed on the hands and feet. These continued to form, especially after bathing; the slightest trauma would produce them. They would

25. Colombini, P.: Beitrag zum Studium der Epidermolysis Bullosa Hereditaria, Monatschr. f. prakt. Derm. **30**:457, 1900.

26. Bonaiuto, F.: Epidermolysis Bullosa Hereditaria, abstr., Brit. J. Dermat. **5**:318, 1893.

persist for a day or two, rupture, and then dry up. Itching or pain had not occurred at any time.

The first set of teeth, which had appeared at the age of 9 months, were friable. The second set of teeth appeared at the age of 5 years and were irregular and widely spaced.

Examination.—General physical examination revealed a boy, aged 9, poorly developed and poorly nourished, with a generalized bullous eruption, especially on the hands and feet. There was no history of alopecia or of development of bullae on the scalp. At the time of examination, there was a mild seborrhea. There were a few atrophic and pigmented patches around the mouth and a few bullae on the ears and cheeks.

Course.—In January, 1926, there were a few small bullae on the lids. The pupils reacted to light and in accommodation. Conjunctivae were normal. There was a small bulla on the left side of the nose. The nasal mucosa was normal.

The teeth were in poor condition, and numerous caries were present. The lateral incisors were set up high in the gums. A roentgenogram of the teeth

Fig. 1.—Bullous lesions on the tongue.

did not show any abnormalities. There were several small, flat-topped bullae on the dorsum of the tongue with several superficial erosions at the edges. The buccal mucosa showed a few erosions, especially along the line of the teeth. The tonsils and adenoids were markedly hypertrophied, so that examination of the larynx, pharynx and esophagus could not be made.

The thyroid, thymus and pituitary glands were clinically and roentgenologically normal.

The skin on the chest and the back were covered with scattered bullae of various sizes, which were interspersed with areas of pigmentation from old lesions.

The lungs, heart and abdomen were normal.

The results of the neurologic examination were negative, except that the reflexes were hyperactive.

The backs of the hands and fingers were covered with numerous bullae of various sizes; several had hemorrhagic contents. The bullous eruption was also marked on the toes and on the dorsum of the feet. The toes had rarely been free from bullous lesions.

The urine was normal on several examinations. The blood count on Nov. 1, 1927, was as follows: white blood cells, 17,200; red blood cells, 4,260,000; hemoglobin content, 54 per cent. The differential count revealed: polymorphonuclears, 77 per cent; lymphocytes, 15 per cent; large mononuclears, 7 per cent, and eosinophils, 1 per cent. The chemical analysis of the blood revealed: nonprotein nitrogen, 31 mg. per hundred cubic centimeters; sugar, 97.5 mg. per hundred cubic centimeters. The Wassermann test of the blood was negative. The clotting time of the blood was two minutes.

Fig. 2.—Typical lesions on the lower extremities.

ANATOMIC CONSIDERATIONS

As the mucous membranes are a modified continuation of the cutaneous covering of the body, they may be involved in certain diseases of the skin. In the toxic and infectious group may be mentioned pellagra, pemphigus, lichen planus and syphilis. In the group of congenital defects may be mentioned nevi, ichthyosis and epidermolysis bullosa. As the latter is concerned with traumatic stimuli, its manifestations are often present in the mucous membranes.

The oral mucosae are more frequently involved because they are exposed to constant irritation from various sources as in speaking, eating and mastication. The walls of the oral cavity, which are movable except for the hard palate, are lined with mucous membranes which are loosely attached and often subject to trauma. The presence of irregular teeth is also a factor in the production of characteristic lesions. As the tongue is a muscular organ and freely movable, its mucous membranes are frequently subject to irritation. Lesions on the hard palate are rare because of the firm attachment of the mucosa to the underlying periosteum.

The larynx and pharynx are less subject to irritation, and therefore lesions are rare in this location. The lining of the esophagus, which is thick and strong, is infrequently affected. Involvement of the anal canal is also rare, because its mucosa is firmly adherent to the underlying muscular structures and is thicker in the canal than in any other part of the large intestine.

SUMMARY

1. A survey of thirty-seven cases of epidermolysis bullosa in the literature revealed that the oral mucous membranes were affected in twenty-seven of the cases, the throat and pharynx in three, the esophagus in two, the eye in three, the anus in two and the penis in four. In several of the cases, there was multiple involvement.

2. The twenty-seven cases in which the oral mucosae were involved included sixteen cases with involvement of the tongue, fifteen cases with involvement of the buccal membranes, six cases of the gums, five of the palate and seven of the lips.

3. A case is reported in which lesions were present on the tongue and on the buccal mucosae.

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MULTIPLE TUMORS OF THE SKIN RESEMBLING MYCOSIS FUNGOIDES

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Mycosis fungoides is a term applied to a clinical syndrome which includes a variety of cutaneous manifestations. Fraser has recently imparted fresh impetus to the pathologic study of this disease. His conclusion, from the study of certain types of this condition, is that its pathogenesis rests in the perivascular reticular system of the skin. This theory places the origin of mycosis fungoides in the papillary layer of the cutis.

The difficulty encountered in the clinical diagnosis of mycosis fungoides is exhibited in a case described in this paper. The patient was presented before the Chicago Dermatological Society at the November meeting, 1926, at which time all of the members present concurred in the diagnosis, but the histologic picture in the case is, in my opinion, incompatible with this diagnosis.

REPORT OF CASE

History.—C. C., a white man, aged 60, a chauffeur, was admitted to the Alexian Brother's Hospital on Aug. 21, 1926, with an oval ulcerating lesion on the right shoulder. One year previously, some red lumps had appeared on the right shoulder, not accompanied by pain or itching. A few months later more lesions appeared on the body, and by June the large ulcer mentioned had formed. In addition to the ulcer on the right shoulder, about twelve nodules were scattered over the body, some of which had ulcerated.

Since that time, the patient had lost 74 pounds (33.6 Kg.) in weight and he felt weak and had no appetite. He complained of pain only when the dressings were changed. Clinical improvement followed the injection of various fever-producing substances and a mild attack of erysipelas of the face.

Laboratory Observations.—The Wassermann reaction of the blood was negative. The urine was normal throughout the course of the disease. Contrasting with the almost normal reactions of the blood in August, 1926, was the blood count in May, 1927, which revealed red corpuscles, 2,888,000; leukocytes, 5,400; and hemoglobin content, 55. The differential count was: polymorphonuclears, 81; lymphocytes, 15; eosinophils, 2; transitionals, 2; and numerous poikilocytes.

On May 4, 1927, the blood pressure was systolic, 126; diastolic, 72; the temperature was 99.4 F., the respirations 18 and the pulse rate 88.

Treatment.—Throughout his stay in the hospital the patient received roentgen-ray treatment, after which the lesions usually healed quickly. Many lesions, which were not treated in this manner, involuted spontaneously. The patient never complained of itching or pain.

Cutaneous Examination.—In August, 1927, the entire cutaneous surface was dotted with tumors and ulcers, which were so numerous on the legs that normal

skin was not visible. A foul smell emanated from these ulcers. The tumors were irregularly shaped and varied in size from that of a pea to that of a thimble. They were solitary and also in groups. The majority of these nodes were elevated, dome-shaped, rose-violet and covered with a smooth epidermis, but some had undergone central eczematization or were umbilicated, presenting a tomato-like appearance. Red-brown flat areas marked the sites of the lesions that had involuted.

In addition to these tumor-like growths, there were many irregularly circular, ulcerating, fungoid lesions, from 1 to 5 cm. in diameter. All of these ulcers presented a distinct, elevated, hard border.

Microscopic Examination.—A tumor the size of a small beech-nut was excised from the right arm. This growth was undergoing central eczematization and was ready to break down. In a section from this tumor, the epidermis was missing in the central portion. The intact epidermis was normal in thickness, and the basal cells showed frequent mitosis. Extending from the epidermis into the subcutis were dense masses of large, pale cells, which were arranged in columns separated from one another by delicate strands of connective tissue (fig. 2). Crowded in between these cells were a few small, dark-staining lymphocytes. The large

Fig. 1.—Appearance of forearm showing domeshaped tumors.

cells had a delicate cytoplasm and round or oval nuclei with loose chromatin granules and small nucleoli. They showed many mitoses with deeply stained chromosomes (fig. 3). There was marked swelling of the collagen in many parts of the cutis.

A section stained with resorcin fuchsin, after Pronter, showed clumping of the elastic fibers in the papillary body.

In a specimen removed from an early node, the same large cells were seen only in the upper portion of the cutis, contiguous to the epidermis.

This microscopic picture was essentially that of a neoplasm. The large cells with the reticular nuclei impressed every observer as being tumor cells. The general impression gained was that one was looking at a new growth, and there was a modicum of inflammatory reaction. One does not associate this picture with that of a granuloma. The slight inflammatory features may be considered as a reaction to the development of tumor cells.

The origin of the large anaplastic cells, commonly found in mycosis fungoides and similar conditions, has been a matter of speculation. Most authorities have maintained that they arise from cells of the lymphocytic series. Fraser suggested that these cells spring from the

reticulum of the perivascular lymphatic tissues in the skin. Sections taken from the small, young nodes of this patient consistently demonstrated the presence of the tumor cells only in the papillary body contiguous to the epidermis.

In the present case, the tumor cells seemed to have developed in close connection with the basal layer of the epidermis. Furthermore, these

Fig. 2.—Masses of large, pale cells.

cells did not appear to be components of the perivascular element, for they had not arranged themselves around the vessels of the cutis.

In true cases of mycosis fungoides and lymphogranulomatosis, many polymorphonuclear eosinophils are usually seen in the microscopic specimens. The absence of these cells in this case, as shown in figure 3, is noteworthy.

HISTOGENESIS OF TUMOR CELLS

Both the clinical and the histologic aspects of the case gave rise to a diversity of opinion. Different observers entertained greatly contrasting ideas about the histogenesis of the large cells characterizing the lesions in this patient. Of these numerous hypotheses, the following four theories were discussed.

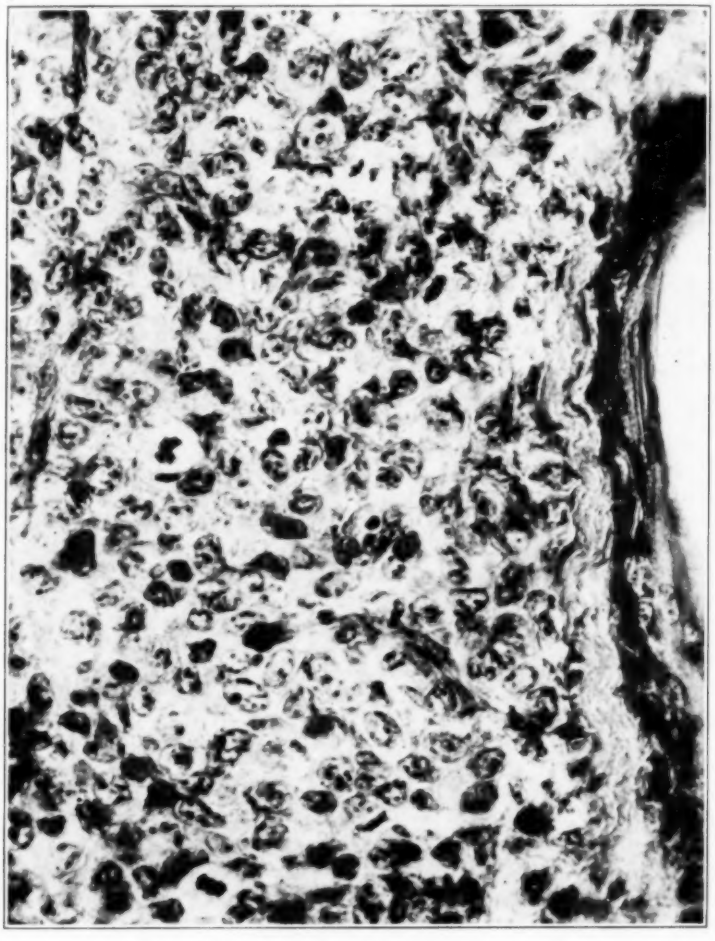

Fig. 3.—Large cells with frequent mitoses.

The diagnosis of the case originally made by several dermatologists was mycosis fungoides d'emblée, and the majority of observers favored this diagnosis throughout the course of the disease. Their belief was that the clinical features established the diagnosis and that the histologic picture was identical with that described by Fraser, who interpreted the origin of the large cells as taking place in the perivascular reticular system of the skin.

However, the solid masses of polygonal cells with vesicular nuclei (fig. 3) impressed Simonds differently. The presence of many mitoses and the character of the edge of the growth indicated to Simonds that the tumors were taking on malignant characteristics, for he had thought at first that the lesion was a lymphoangio-endothelioma of the skin, and this growth is usually benign.

Jaffé thought that the cells were mesenchymatous in origin and that the neoplasm belonged to the group of multiple sarcomas of the skin. His idea was that the tumor nodes might arise in the subepithelial layer of the cutis and at a very early stage invade the epithelium.

Finally, an entirely new aspect to the problem was furnished by Sternberg of Vienna, who expressed the belief that the large round cells in the case were derived from the epidermis. According to him, the condition was multiple, immature carcinoma of the skin. It is known that this type of epithelial proliferation sometimes resembles round cell sarcoma. Sternberg pointed out the close topographic relationship of the cells under discussion to the epidermis and the occurrence of numerous mitotic figures with short and slender chromosomes in the cells of the rete malpighii.

In my material, the tendency of the collagen to swell and become homogeneous has been noted. In accordance with Sternberg's idea, this fact is important. Bierich and Kyrle were struck with this change in their specimens of incipient carcinoma of the skin and even went so far as to say that such an alteration in the collagen precedes epithelial proliferation.

SUMMARY

The clinical picture of the case is that of a multiple tumor-like lesion of the skin. The early lesion was a pea-sized, rose colored, hard and superficial nodule, freely movable in the skin. The color grew deeper under the pressure of a glass slide. This nodule increased in size, and when ulceration occurred, a hard, translucent and elevated border defined the lesion from the surrounding normal skin.

The absence of itching throughout the course of the disease was noteworthy. In all, except the d'emblée type of mycosis fungoides, pruritus is the dominant, almost refractory complaint. In Fraser's third patient, suffering from what he designated as lymphosarcoma, which resembles this case closely, itching was absent.

Many of the lesions underwent spontaneous involution, so characteristic of mycosis fungoides. Is this fact tenable with an epithelial genesis? Certain authorities maintain that the multiple basal cell epitheliomas, which Arning, Arzt and I call carcinoids, can undergo spontaneous resolution. As in this type of tumors, the lesions regress

rapidly with roentgen-ray treatment. Pusey tells of a woman afflicted with multiple cutaneous epitheliomas in whom the lesions disappeared without treatment.

Such an hypothesis *a priori* excludes the possibility that the lesions under discussion are granulomas. The small amount of inflammatory features seems to represent a weak defensive inflammatory reaction on the part of the tissues. According to my interpretation of the lesions in this type of hyperplasia, the nature of the process must be construed as truly neoplastic from beginning to end.

CONCLUSION

A case of multiple tumors of the skin resembling mycosis fungoides d'emblée is described.

The great difficulty in determining the exact nature of these lesions is emphasized.

These lesions are, without doubt, true tumors, most probably a peculiar type of carcinomatosis cutis.

The tissue changes in this case are not those of mycosis fungoides, which is an inflammatory condition and belongs to the class of specific granulomas. Mycosis fungoides in its classic sense is characterized by the great variety of cells, notably a peculiar type of giant cell.

SARCOIDS AND RELATED LESIONS

REPORT OF SEVENTEEN CASES; REVIEW OF RECENT LITERATURE *

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With Boeck's [1] description of the sarcoids, a morphologic entity was admittedly established. It soon became apparent, however, that his conception of the eruption was not sufficiently inclusive, as evidenced by the acceptance of a subcutaneous type referred to as the Darier-Roussy type. Later, Darier [2] classified sarcoids into four types. As experience with these nodular lesions grew it became apparent that a sharp dividing line could not be drawn, except that Darier's type 4 has been rather definitely eliminated from this group since it probably is a lymphoblastomatous disease. Both Boeck and Darier believed the sarcoids to be tuberculous in origin. Further study contributed much evidence to this belief, but it also indicated that other nodular cutaneous lesions, for example, lupus pernio [3] (not the chilblain lupus of Hutchinson) and erythema induratum, were closely related to the sarcoids, so much so that Lewandowsky [4] and Kyrle [5] have coined the inclusive term "tuberculosis cutis indurativa" for this entire group.

It cannot be said, however, that this conception has been as yet universally accepted. Some of the dermatologic textbooks still refer to Darier's classification as though it were a standard by which the sarcoids should be measured. In the society meetings rather sharp differentiation is often insisted on to the point that some feature not conforming to the original description of one of the subgroups will elicit much discussion. In the material at the Mayo Clinic, it is significant

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* Read before the American Dermatological Association, Washington, D. C., April 30-May 2, 1928.

1. Boeck, C.: Multiple Benign Sarkoid of the Skin, J. Cutan. Dis. **17**:543, 1899.

2. Darier, J.: Die cutanen und subcutanen Sarkoide: Ihre Beziehungen zum Sarkom zur Lymphodermie, zur Tuberkulose, u. s. w., Monatsch. f. Prakt. Dermat. **1**:419, 1910.

3. Jadassohn, J.: Sarkoide und Lupus pernio, Cor.-Bl. f. schweiz. Aerzte. **44**:1475, 1914; in Mraček, Franz: Handbuch der Hautkrankheiten, Vienna, Alfred Hölder, vol. 4, 1907, p. 177.

4. Lewandowsky, F.: Tuberkulose-Immunität und Tuberkulide, Arch. f. Dermat. u. Syph. **123**:1, 1916; Zur Kenntnis der Boeckschen Sarkoide, Arch. f. Dermat. u. Syph. **135**:287, 1921.

5. Kyrle, J.: Die Anfangsstadien des Boeckschen Lupoids; Beitrag zur Frage der tuberkulösen Aetiologie dieser Dermatose, Arch. f. Dermat. u. Syph. **131**:33, 1921; Ueber die tuberkuloiden Gewebsstrukturen der Haut, Arch. f. Dermat. u. Syph. **125**:481, 1920.

that in practically all cases in which the sarcoids came into question multiple diagnoses head the history sheet, and these practically always refer to two or more of the related subgroups. From the comments on the history sheet, it is evident that one or the other clinical or even a histologic feature of the case would not permit a definite diagnosis. In an endeavor to show the futility of drawing a sharp dividing line between these groups, I shall first report pertinent cases from my own experience, and then analyze them in the light of experience as reported by others in the literature.

REPORT OF SEVENTEEN CASES

CASE 1.—A woman, aged 28, entered the clinic in August, 1920. There were doughy, nodular, purplish infiltrations on the thumb and index finger of the left hand, on the upper right arm at the insertion of the deltoid, on the left malar prominence, and on the tip of the nose. Some of the lesions showed telangiectatic vessels, but there were no definite grayish-brown nodules on pressure. The mucous membrane was not involved. The first lesion had appeared on the thumb at the age of 21, the lesion on the arm at 24, and the lesions on the nose and cheek at 26 and 27, respectively. The patient had always considered her general health to be good.

Roentgen-ray examination of the lungs showed old tuberculous lesions of both upper lobes, and an unusual diffuse miliary infiltration in both lungs, a dense bronchial infiltration radiating from the tubes, and possibly bronchiectasis (fig. 1). Roentgen-ray examination of the bones of the hands and feet showed fibrocystic changes (fig. 2). There were, also, atrophic rhinitis and moderate enlargement of the axillary lymph nodes; the spleen was palpable. Arsenic in the form of solution of potassium arsenite and neoarsphenamine did not prove of value; neither did potassium iodide. Radium improved the lesions somewhat, but was not especially satisfactory. General tonic measures later gave the best results, however, without bringing about complete disappearance of the lesions. The microscopic section was typical but would not permit differentiation of the sarcoids and lupus pernio, except possibly for the dilatation of the superficial vessels (fig. 3). Neither would the section alone exclude erythema induratum, although the vascular involvement is usually more in evidence than was found in this case.

An almost identical clinical picture was presented by case 2.

CASE 2.—A woman, aged 42, came to the clinic in 1924. Lesions had appeared on the fingers at the age of 36; after several years they appeared on the face, and somewhat later on the arms and trunk (fig. 4). The lesions were purplish and doughy; at first they were evidently rather deep-seated but gradually approached the surface. One examiner thought they resembled deep vascular nevi. The surface of a number of the lesions was telangiectatic. There was no definite evidence of tuberculosis. The patient's general health had aways been good.

A history of iritis was elicited and residual scarring was still present. The iritis was active before the first lesions appeared on the fingers. A roentgen-ray examination of the bones showed fibrocystic disease in the phalanges of both hands. Lesions were not present in the lungs. The eruption did not respond to a solution of potassium arsenite or to Asiatic pills. One of the lesions recurred after excision. A section removed for microscopic study corresponded with the picture seen in the group of cases under discussion.

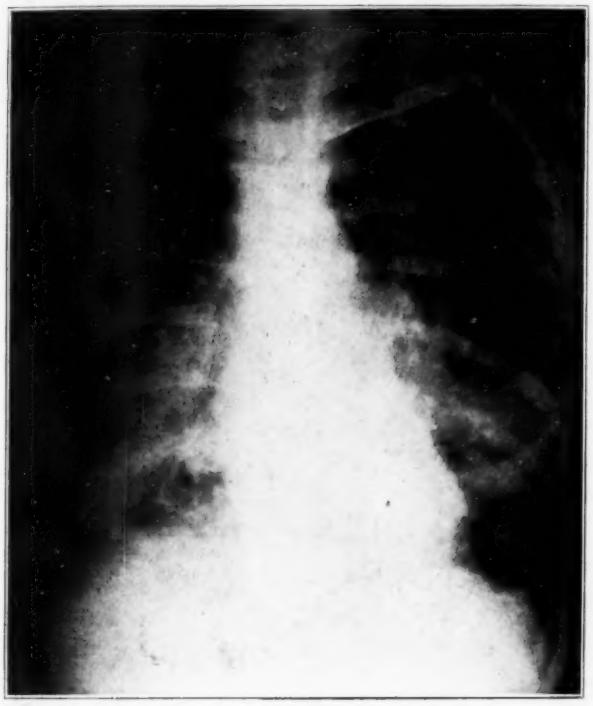

Fig. 1 (case 1).—Infiltration of lungs.

Fig. 2 (case 1).—Fibrocystic changes in bases of fingers.

The condition in case 3 resembled that in cases 1 and 2 from the cutaneous standpoint but differed in that active tuberculosis was present.

CASE 3.—A woman, aged 54, was first seen in the clinic in 1922. A lesion had appeared on the left cheek at the age of 48. Later, other lesions appeared on the nose and upper lip. Her general health had been poor for many years.

A roentgen-ray examination showed fibrotic infiltration of the lungs and fibrocystic degeneration of the fifth metatarsal phalanges of both feet and destruction of the first phalanx of the middle finger of the left hand. There was active tuberculosis of the pharynx and larynx. Arsenic was not tried in this case. A biopsy was not made.

Case 4 probably may be classified with cases 1, 2 and 3.

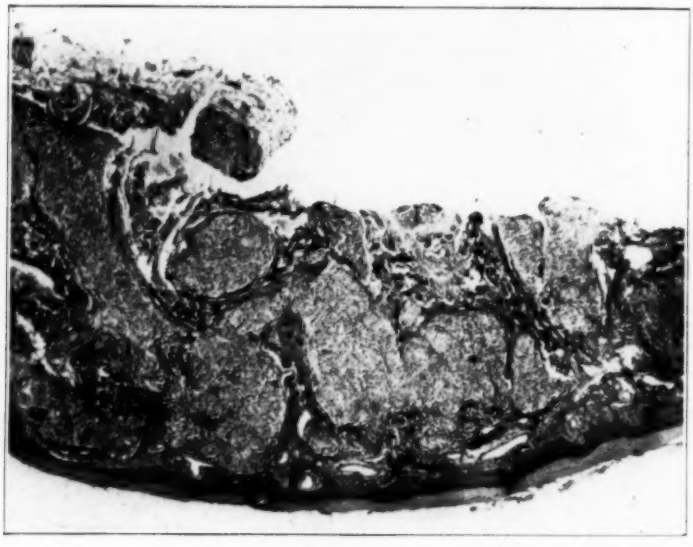

Fig. 3 (case 1).—Section of lesion. Typical sarcoid infiltration; dilated vessels in spears papillares.

CASE 4.—A boy, aged 13, was first seen in the clinic in 1925. A purplish lesion with telangiectasia that suggested lupus pernio had been present for two years. There were definite changes in some of the phalanges of the fingers (fig. 5). At the age of 8, following an injury to the back, an indolent ulcer developed with discharge of much pus. Later, ulcerating lesions appeared on the left thigh and in the left groin. These lesions were probably colliquative tuberculosis.

A roentgen-ray examination showed fusion of the third and fourth lumbar vertebrae which had probably followed tuberculosis of the vertebrae. The roentgen-ray examination of the chest showed some bronchial thickening.

As a contrast to the foregoing cases which could be classified as lupus pernio without great difficulty, particular attention is directed to case 5. This case illustrates well the impossibility of always drawing a sharp dividing line in the nodular lesions under discussion.

CASE 5.—A man, aged 54, was first seen in 1920. At that time he had various indefinite complaints; he feared that he had tuberculosis, and seemed rather dull mentally. A few crackles were noted over the apex of the left lung posteriorly. Because of some irregularity and sluggishness in reaction of the pupils, syphilis was suspected, but could not be proved on careful study. He was seen in March, 1921. The crackles over the apex of the left lung were again noted and the patient complained a great deal of parosmia. Cutaneous lesions were not present and a definite diagnosis was not made. In January, 1927, he returned for examination. The parosmia had disappeared but he complained of nasal obstruction. His general condition had improved. He gave a history of periodic transient enlargement in the parotid region for the last ten or fifteen years. To

Fig. 4 (case 2).—Distribution of lesions.

his knowledge, there never had been enlargement of the lymph nodes about the head or neck.

On examination, palpable lymph nodes were not found anywhere. The spleen seemed somewhat enlarged and tender. In both parotid regions, involving only the skin and subcutaneous tissues, were indurated plaquelike lesions from about 3 to 6 cm. in diameter (fig. 6). These were purplish with much more of the bluish than the brownish tint. Diascopic pressure did not show any of the well known yellowish-brown nodules seen in Boeck's sarcoid and less pronounced in lupus pernio. The surface was covered with a fine network of dark blue dilated vessels, varying somewhat in size and larger in the center than at the periphery. The induration was nodular rather than uniformly smooth and plate-like. It was doughy at the periphery but became almost cartilaginous toward the center. Central clearing and ulceration were not noted. A similar lesion, more

round in appearance and not so hard, was found in the left lower costal region posteriorly. Many lipomas varying in size from 0.5 to 5 cm. in diameter were found everywhere on the body except on the head and the palms and the soles. Roentgen-ray examination showed small nodular infiltrations in the lungs which reminded the examiner of the metastasis of a malignant infection, but evidently they were the lesions not uncommonly associated with sarcoids and lupis pernio (fig. 7). Examination of the ears, nose and throat showed indurated symmetrical hypertrophy of the lacrimal glands and atrophic rhinitis. The hemoglobin was 58 per cent, the erythrocytes numbered 3,230,000 and the color index was 0.8+. The split blood cholesterol showed 55 mg. per hundred cubic centimeters, and there was an increase in the total cholesterol of the blood. The Mantoux test was negative in the normal and pathologic skin. A subcutaneous injection of 0.5 mg.

Fig. 5 (case 4).—Injury to bone especially noticeable in first phalanxes of middle finger of left hand.

of old tuberculin did not give any reaction. Guinea-pig inoculation with tissue obtained from the lesion on the trunk was negative.

A specimen excised from the lesion on the trunk showed slight infiltration in some places in the upper corium, chiefly of a perivascular type. The epidermis was essentially normal. The infiltration was dense in the lower cutis and subcutis and involved the fatty layer extensively by proliferation atrophy. The infiltration in the upper layers of the deeper cutis was moderate and consisted chiefly of leukocytes. The lower layers showed a marked predominance of epithelial cells in the round and oval nodules. The nodules were sharply outlined by connective tissue septums. Some nodules consisted exclusively of epithelioid cells, others were tuberculoid with epithelioid cells in the center surrounded by a halo of lymphocytes. Occasionally, a considerable part of the nodule was made up of lymphocytes. Giant cells were rare but a number of typical Langhans' cells were found. The atypical types were seen more often, especially in the proliferation

atrophy of the fatty tissue. Occasionally, a number of atypical giant cells were seen in a small focus. Plasma cells were exceedingly rare and mast cells were not found. The vessels of the upper corium showed moderate changes only; occasionally, there was slight endothelial proliferation and thickening. While some vessels showed little change, others showed enormous thickening and abundant endothelial changes. Total occlusion of the vessels was rarely noted. The collagen and elastic fibers were entirely destroyed within the nodules, but were normal otherwise. There was also marked destruction of the sweat glands but little involvement of the sebaceous glands, possibly because of the predominance of the infiltration in the deeper layers of the skin. A diligent search for the bacilli of tuberculosis in a considerable number of serial sections did not reveal any. Sections were stained by the carbol fuchsin, van Gieson, hemotoxylin-eosin, and acid orcein polychrome methylene blue methods. Similar results were

Fig. 6 (case 5).—Lesions on the cheek.

obtained in a section taken from one of the lesions on the cheek only in this case, the infiltration was more superficial. Removal of one of the noninflammatory fatty tumors from the arm and another from the trunk showed the typical structure of a lipoma. There was no increase in the interlobar connective tissue nor was there any increase of cells suggesting inflammatory reaction.

Case 6 also shows the difficulty of making a definite subclassification.

Case 6.—A man, aged 44, was first seen in the clinic in 1924. Lesions of the skin were confined to three definite areas: on the inner side of the knees, on the posterior aspect of the calves near the ankle, and on the buttocks. Objectively, the lesions near the knee resembled the lesions of a Boeck's sarcoid or lupus pernio. The lesions near the ankles had more the appearance of erythema nodosum; those on the buttocks resembled those on the ankle; the latter, however,

had occasionally broken down and discharged. The patient said that he had had similar lesions on the hand about thirteen years previously and one lesion on the face about three years previously. Leukemia, leprosy, syphilis and paraffinoma were carefully excluded.

Microscopic examination showed rather marked infiltration of the upper cutis with epithelioid cells, particularly surrounding the blood vessels and extending close to the epidermis. There was some lymphocytic infiltration also, but it was negligible in amount; giant cells were not found. The deeper layers of the cutis were not invaded and the epidermis was essentially normal.

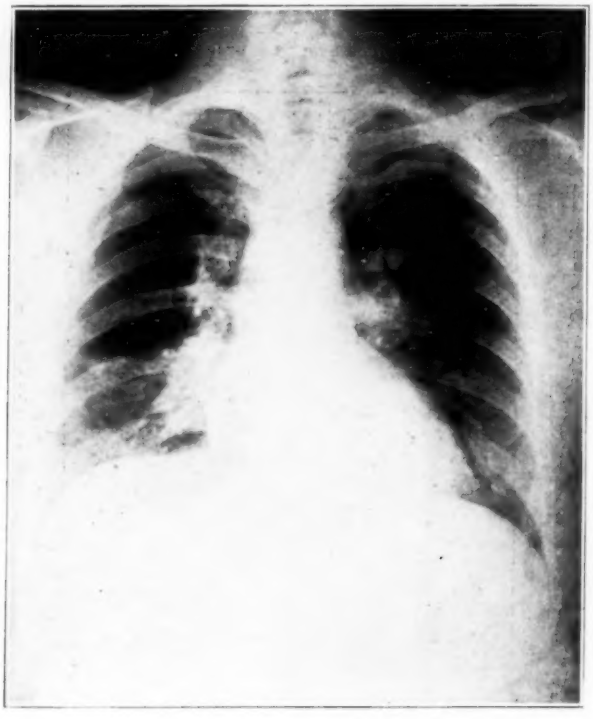

Fig. 7 (case 5).—Infiltration in lungs.

Cases 7 and 8 can be readily classified, by their morphology, with the sarcoids. They especially illustrate the necessity of recognizing the associated systemic symptoms.

Case 7.—A woman, aged 48, was first seen in the clinic in 1920. The first lesion was noticed on the upper part of the right arm at the age of 44; a little later a lesion appeared on the right cheek. Other lesions gradually appeared on the left forearm, the right thigh and the lower part of the left leg. Except for the lesion on the face which resembled Boeck's sarcoid, the appearance of the lesions suggested erythema nodosum. Before lesions appeared on the skin, the patient had noticed irregularity of menstruation beginning at the age of 40. Since she was 44 she had had periodic attacks of vomiting with jaundice. At 40,

she had noticed enlargement of the cervical lymph nodes with protrusion of the eyes. Enlargement of the spleen was noticed at 45.

The question of whether any of these symptoms had any direct relationship to the sarcoids must remain unanswered. At the time of examination, generalized superficial adenopathy, bilateral chronic parotitis, and splenomegaly were noted. All these signs have been reported associated with Boeck's sarcoid and are probably part of a syndrome. Arsenic was not tried in this case.

CASE 8.—A woman, aged 57, was examined at the clinic in 1924. The first lesion had been noticed on the right cheek three years previously; soon after another appeared in the right cervical and left sternoclavicular regions. These

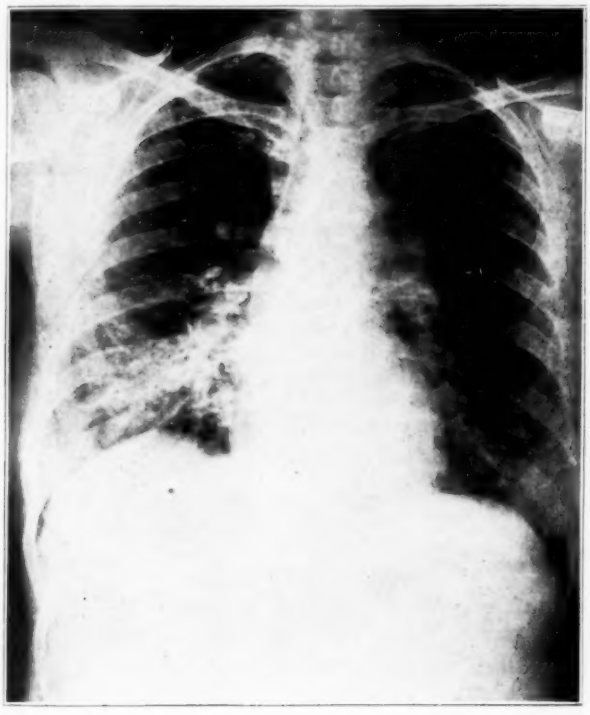

Fig. 8 (case 8).—Marked infiltration in lungs.

lesions answered to the description of Boeck's sarcoid. The patient had felt that she was in good health until the lesions appeared. There were nodular infiltrations in the lungs similar to those in cases 1 and 5 (fig. 8). Hypertrophic arthritis of the lumbar spine was discovered, but fibrocystic disease of the bones was not elicited. There was also rather marked splenomegaly. Jaundice had appeared at the age of 55 and had been present until two months before examination. Vomiting or nausea had not occurred.

The use of neoarsphenamine was advised, but the patient did not cooperate in treatment. A microscopic examination of a section in this case showed the typical picture of Boeck's sarcoid.

Case 9 is noteworthy because of the situation of the lesions.

Case 9.—A man, aged 32, was seen in 1921. The first lesion appeared on the soles at the age of 25, and had remained. Systemic symptoms or signs were not present. Treatment with arsenic was not given. The section for microscopic examination showed at least one nodule typical of a Boeck's sarcoid, but the epidermis was markedly acanthotic (figs. 9 and 10).

In the remaining cases (cases 10 to 17), the clinical appearance and behavior were fairly typical of Boeck's sarcoid. Certain points, how-

Fig. 9 (case 9).—Typical rather deep seated sarcoid nodule.

ever, will bear emphasis, especially the associated tuberculosis and the reaction to arsenical medication.

Case 10.—A woman, aged 40, was seen in 1926. A typical lesion had appeared on the left cheek about a year previously. There were no subjective symptoms. The lesion did not respond to the administration of arsphenamine or a solution of potassium arsenite.

Case 11.—A woman, aged 32, was seen in 1920. The first lesion had appeared on the forehead about two years previously. It gradually spread until at the time of examination it presented a typical plaquelike Boeck's sarcoid; this was confirmed by microscopic examination. There were no systemic symptoms. Roent-

gen-ray examination disclosed old tuberculous lesions of the lungs. The patient did not take treatment.

CASE 12.—A man, aged 30, was seen in 1923. A plaquelike sarcoid resembling Boeck's type was first noticed in 1918 over the glabella. The lesion had not responded to any efforts at treatment including excision. There were no systemic symptoms. Roentgen-ray examination disclosed an old tuberculous lesion of the lungs. The patient was treated for several months with a solution of potassium arsenite, Asiatic pills, and neoarsphenamine. Kromayer light, with pressure, was also used. Response was not satisfactory. The microscopic section was rather atypical of sarcoid.

Fig. 10.—Acanthosis.

CASE 13.—A woman, aged 54, was seen in 1926. The first lesion on the skin of the face had appeared three years previously. Later, similar lesions appeared on the scalp, ears, neck, arms and legs. The only systemic symptom was a general lack of vigor. A roengen-ray examination disclosed old tuberculous lesions of the upper lobes of both lungs. Evidence of old uveitis was also found. The lesions disappeared promptly under the use of the Kromayer lamp and neoarsphenamine. Microscopically, a section was typical for sarcoid.

CASE 14.—A woman, aged 35, was seen in 1920. The first lesion had appeared in the right temporal region about a year previously. This disappeared and a new lesion soon appeared just under the right eye. The lesions were large and nodular. The largest was the one under the right eye, but there were several

smaller ones under the left lid and another on the left cheek nearly as large as the one on the right side. There were no systemic complaints. Roentgen-ray examination disclosed an old tuberculous lesion of the upper lobe of the right lung. The lesions disappeared slowly but completely under a course of arsphenamine.

Case 15.—A man, aged 35, was seen in 1924. The lesions had first appeared about four years previously on the back; they were of the small nodular type. The patient came for examination because of abdominal complaint. An operation disclosed tuberculosis of the cecum. Nothing is known of the subsequent course.

Case 16.—A man, aged 41, came for examination because of lesions on the left cheek, which had appeared first two years previously; others on the right

Fig 11 (case 17).—Typical rather deep-seated infiltration.

cheek appeared a year later. There were no systemic symptoms. Clinically and microscopically, the lesions were typical. Arsenic in the form of a solution of potassium arsenite did not change the condition.

Case 17.—A woman, aged 41, who was examined, gave a history of the appearance of lesions on the right cheek five years previously; somewhat later, lesions appeared on the left cheek, and then gradually others appeared on the shoulders, arms and trunk. Clinically, the lesions lacked the peculiar doughy or even cartilaginous infiltration. They were purplish and some of them were suggestive of erythema multiforme. The microscopic sections, however, showed definite infiltration as seen in Boeck's sarcoids principally of the deeper type (fig. 11). Arsenic was not tried.

CLASSIFICATION

Certain observers today group the sarcoids of Boeck and Darier-Roussy and lupus pernio and erythema induratum under one heading. They believe that the bacillus of tuberculosis is the causative agent and that the reason for the characteristic nodules, as distinguished from other tuberculosis lesions, lies in the high degree of allergy, or possibly anergy, in cases presenting these lesions. The belief in their essential identity is materially strengthened by the similarity of the histologic changes which resemble each other so closely, even when the clinical picture varies considerably, that differentiation by microscopic examination is impossible. Furthermore, there are cases that clinically do not fit the description of any of these groups, and yet their histologic features are the same. Such cases have been presented by Weidmann [6] and Wright [7] in this country, and by Jadassohn and Kuznitzky [8] in Germany. In contrast, Fox and Wile,[9] as early as 1911, called attention to a typical case of Boeck's sarcoid with atypical features histologically. Foerster,[10] Stokes,[11] and others have called attention to the probability that in some instances erythema nodosum may be tuberculous in origin. Clinically, cases of this condition sometimes resemble sarcoid or erythema induratum and would probably have to be classified with these groups were the dividing line not too sharply drawn. Indeed, Bazin probably included this type in his original description. In 1911, Wende [12] described nodular lesions of the skin which he called "nodular tuberculosis of the hypoderm." It is difficult to see wherein the condition in his case differs from Boeck's sarcoid. The distribution, the size, the spread and the histologic picture, all are compatible with the sarcoids. Wende himself saw a close relationship to erythema induratum except for the distribution, absence of ulceration, and the ease with which he found the bacilli of tuberculosis. Only the last feature would be of decisive value in differentiating the condition from sarcoid. At present,

6. Weidmann, F. D.: Sarcoid of Boeck and Lichen Scrofulosorum-Arsphenamin Treatment, Arch. Dermat. & Syph. **5**:423, 1922.

7. Wright, C. S.: Lichenoid Sarcoid, Arch. Dermat. & Syph. **12**:374 (Sept.) 1925.

8. Kuznitzky: Lungenveränderungen bei Boeckschem Sarcoid resp. Lupus pernio, Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:563, 1919.

9. Fox, G. H., and Wile, U. J.: Sarcoid Tumors of the Skin with Report of a Case of the Boeck type, J. Cutan. Dis. **29**:375, 1911.

10. Foerster, O. H.: The Association of Erythema Nodosum and Tuberculosis, J. A. M. A. **63**: 1266 (Oct. 10) 1914.

11. Stokes, J. H.: Erythema Nodosum, Tuberculosis; Report of a Case Terminating in Tuberculous Meningitis with Necropsy, Arch. Dermat. & Syph. **3**:29 (Jan.) 1921.

12. Wende, G. W.: Nodular Tuberculosis of the Hypoderm, J. Cutan. Dis. **29**:1, 1911.

however, this has also lost much of its value since Kyrle has shown that the bacillus of tuberculosis can be found only if at all, in the earliest lesions of sarcoid. It is probable that Wende was the first to demonstrate the bacilli in early sarcoid without being aware of it.

Those opposed to the tuberculous nature of the sarcoids will, of course, not be willing to accept the identity of these diseases. Those who believe that some of the cutaneous lesions are entities will draw a sharp dividing line. Kuznitzky and Bittorf,[13] when reporting the first case of sarcoid with systemic symptoms, believed that they were dealing with a disease sui generis. In reporting a case, Rischin [14] also subscribed to this opinion. The other view, that these lesions are the result of various causes even when clinically and histologically similar, still has adherents, although these would probably not be willing to establish any exact classification, but merely to view the lesions as symptomatic manifestations of various diseases. The mere fact that each of these three opinions still has its champions is evidence that sharp dividing lines can be drawn only with the greatest difficulty either clinically or histologically. The matter of classification of this variety of skin lesions is further complicated by the presence of associated systemic lesions in some cases, and their absence in others. The nodules described in the lungs, fibrocystic disease of the bones, splenomegaly, adenopathy and other conditions may be associated with various lesions of the skin. Fortunately, the problem of differentiation of lesions of the skin usually lies (in the latter group only) between the sarcoids and lupus pernio. If a common etiologic factor with a similar genetic mechanism is conceded, such associated systemic lesions and their common repetition with rather characteristic skin lesions may be explained simply. If, however, it is assumed that sarcoids with systemic lesions as compared with identical lesions without systemic lesions, or that varying skin pictures as represented by the various forms of sarcoids and lupus pernio associated with the same systemic lesions represent different entities, the problem of classification becomes greatly involved. I prefer to explain the presence or absence of these systemic lesions with variations in the appearance of the skin lesions by assuming a common tuberculous etiology but a difference in the patients' reactive ability, and in discussing them, I shall refer to them as of tuberculous origin.

The lesions under discussion and the nodular lesions seen in the skin as the result of other definite disease entities, for example, syphilis, leprosy and the lymphoblastomas, must be differentiated sharply. Such lesions may closely resemble the tuberculous lesions clinically and even

13. Kuznitzky, E., and Bittorf, A.: Boecksches Sarkoid mit Beteiligung innerer Organe, München. med. Wchnschr. **62**:1349, 1915.

14. Rischin, M.: Universelles benignes Miliarlupoid Boeck mit Beteiligung innerer Organe, Arch. f. Dermat. u. Syph. **139**:30, 1922.

histologically. It is usually necessary to observe a patient presenting such a diagnostic problem for a long period of time or otherwise to establish the diagnosis by collateral evidence. For instance, a positive Wassermann reaction of the blood and prompt response of the lesions in a given case to a therapeutic test with mercury is the only evidence that will favor a diagnosis of a syphilitic lesion. Such problems, however, are of a diagnostic character and do not contribute to a logical classification of the lesions under discussion, and such lesions should not be classified in the same group with the sarcoids or related tuberculous lesions even if they closely resemble them morphologically and histologically.

There are, no doubt, other nodular lesions the etiology of which is as yet unknown. These may closely resemble the sarcoids clinically but ordinarily they differ histologically. The nodules usually occur in the fatty tissue and have been described by Pfeifer,[15] Kraus,[16] Küttner,[17] Alexander,[18] and others. They have followed trauma, and have been seen in association with cachexia, articular rheumatism and pemphigus. Küttner expressed the opinion that fat crystals acting as foreign bodies and producing a foreign body reaction may be responsible for the lesions. This theory is particularly interesting if some of the problems connected with the cause of sarcoids are considered, and may help to explain the similarity of some other cutaneous nodules to true sarcoids.

DIAGNOSIS

The constant repetition of nodular lesions in the skin similar as to color, consistence, configuration, distribution and behavior, is accepted. In this sense a subclassification into the various types of sarcoid, erythema induratum, and lupus pernio may be justifiable. But it is equally true that many such cases will not present features that are not commonly associated with descriptions given to one of the other subgroups. In 1910, Darier called attention to the fact that the sarcoid of Boeck is clinically a well recognized disease, but that there are transition cases that resemble other tuberculous lesions. In 1915, Zeisler[19] called attention to an uncommon case of multiple benign sarcoid. He

15. Pfeifer, Victor: Ueber einen Fall von herdweiser Atrophie des subcutanen Fettgewebes, Deutsches Arch. f. klin. Med. **50**:438, 1892.

16. Kraus, Alfred: Ueber entzündliche Knotenbildung in der Haut mit umschriebener Atrophie des Fettgewebes, Arch. f. Dermat. u. Syph. **66**:337, 1903.

17. Küttner, Hermann: Ueber circumscripte Tumorbildung durch abdominale Fettnekrose und subcutane Fettspaltung, Berl. klin. Wchnschr. **50**:9, 1913.

18. Alexander, A.: Ueber die Beziehungen zwischen dem Erythema induratum resp. dessen Atypien und den nicht tuberkulösen, entzündlichen Fettgewebstumoren, Dermat. Ztschr. **27**:127, 1919.

19. Zeisler, Joseph: An Uncommon Case of Multiple Benign Sarcoid of the Skin, J. A. M. A. **65**:764 (Aug. 28) 1915.

did not feel that the divergent data should be a surprise as a similar difficulty had formerly been encountered in lupus. Seemingly, he believed that in sarcoid an entity was being dealt with, but he was willing not to draw the line too sharply. He emphasized the possibility of syphilis simulating sarcoid and that the presence of a positive Wassermann reaction and response to arsphenamine does not establish the lesion as syphilitic. He was fully aware of the difficulty of at times differentiating syphilis, lepra, lupus, mycosis fungoides, lymphoderma, sarcomatosis and foreign bodies from the sarcoids. In 1919, Sweitzer and Michelson [20] reported a case of sarcoid that closely resembled erythema induratum. Even then, they emphasized the necessity of simplifying the classification of sarcoids. One readily draws the inference from their article that differentiation is spun too fine among lesions that are probably identical in their essential features. In 1921, Finnerud [21] made a careful clinical, histologic and bacteriologic study of a case of Boeck-Darier-Roussy sarcoid which clinically and histologically would easily fit the description of lupus pernio. In 1922, Lewandowsky [4] reported a case in a boy, aged 12, who had had two attacks that closely simulated erythema nodosum. Microscopic examination of the lesions, however, showed that the condition resembled closely Boeck's sarcoid. To these observations one may add the atypical clinical cases of Weidmann and Wright which microscopically, however, were typical for sarcoid. These observations as found in the literature can, I believe, only be harmonized if it is conceded that the lesions under consideration have a common etiologic factor, but may vary decidedly in their clinical manifestations, and that many cases can be found that have characteristics of one or more of these cutaneous lesions that will not permit of a sharp subgrouping. If this view is not accepted, Weidmann's and Wright's cases would probably each have to be regarded as entities. This conception is further supported by my own experience in the cases reported here. If the older classification is retained, cases 1 to 4 are probably best classified with lupus pernio, although cases 3 and 4 do not present all the classic features. In case 5, the condition resembles both lupus pernio and Boeck's sarcoid, and the lesion on the trunk would answer the description of the Darier-Roussy type. Case 6 resembled Boeck's sarcoid and erythema induratum. Cases 7 and 8 are probably best classified as Boeck's sarcoid with systemic symptoms. Case 9 represents an unusual distribution of a Boeck's sarcoid, but

20. Sweitzer, S. E., and Michelson, H. E.: Sarcoid of Boeck and Erythema Induratum of Bazin, J. Cutan. Dis. **37**:98 (Feb.) 1919. Sweitzer, S. E.: Sarcoid of Boeck, J. A. M. A. **63**:991 (Sept. 19) 1914.

21. Finnerud, C. W.: A Clinical, Histologic, Bacteriologic Study of a Case of Multiple Benign Sarcoid of Boeck-Darier-Roussy, Arch. Dermat. & Syph. **4**:342 (Sept.) 1921.

closely resembles clinically the case reported by Jadassohn. The acanthosis corresponds to the verrucous character in his case, and the deeper infiltration was characteristic. The remaining cases were fairly typical of the sarcoid originally described by Boeck.

Whether or not a morphologic differentiation of the cutaneous eruption is insisted on, one cannot overlook the fact that various lesions of the skin are characteristically associated with systemic lesions. Such cases are most significant because they strongly suggest a disease entity rather than symptoms due to multiple etiologic factors, even if the eruption on the skin varies greatly in its clinical characteristics. On the other hand, if one looks on such cases as representing a disease sui generis, it will be hard to explain the similarity clinically and histologically to skin eruptions without systemic lesions. To assume that multiple etiologic factors should be capable of producing again and again a combination of certain rather striking cutaneous lesions with rather characteristic nodular infiltrations in the lungs, fibrocystic changes in the bones, splenomegaly and adenopathy, would seem far-fetched. For the lesions of the skin alone, multiple etiologic factors would be more plausible as it is not unusual to see the same lesions as signs and symptoms of a number of diseases. A common etiologic agent with the ability to stimulate various degrees of tissue reaction not only in the skin but also, by selecting by preference, in some other tissues, such as bones, lymph nodes and spleen, seems, in the light of present knowledge of immunity reactions, the most plausible. The bacillus of tuberculosis can answer these requirements admirably.

The cases associated with such systemic lesions are of further interest because it is only recently that they are being more commonly recognized. There is little doubt that such lesions will be found more often if they are looked for systematically in every case of sarcoid or lupus pernio or in cases resembling these eruptions. Even the competent internist is unfamiliar with this syndrome and will look askance at an effort to explain the lesions of the skin and the systemic reactions as a disease entity or all of the manifestations as part of the same syndrome. The literature as yet is not abundantly supplied with reports of such cases, but there is enough to show that they may be met with at any time. Kuznitzky and Bittorf reported the first case. Among others who reported cases, I will mention only Kyrle, Schaumann,[22] Lutz,[23]

22. Schaumann, Jörgen: Étude sur le lupus pernio et ses rapports avec les sarcoides et la tuberculose, Ann. de dermat. et syph. **46**:357, 1916-1917; Études histologique et bacteriologique sur les manifestations médullaires du lymphogranulone bénin, Ann. de dermat. et syph. **7**:385, 1918-1919; Sur la nature du "lymphogranulome bénin" à propos d'une observation de lupus perno dans laquelle las lésions pulmonaires étaient causées par le bacille tuberculeux du type bovin, Acta derm.-venereol. **2**:409, 1921.

23. Lutz, Wilhelm: Zur Kenntnis des Boeckschen Miliarlupoids, Arch. f. Dermat. u. Syph. **126**:947, 1919.

Boeck,[1] Bloch,[24] Jüngling,[25] Gans [26] and Lewandowsky.[4] In the series reported in this paper, systemic lesions were found associated with lesions of the skin in cases 1, 2, 3, 5, 7 and 8, six of the seventeen (35 per cent).

It was of interest to note whether any one systemic symptom occurred more frequently or more exclusively in association with any one type of skin lesion. Such peculiar association is not apparent in the literature except so far as the fibrocystic changes of the bone were common with the lupus pernio type of eruption. The outstanding systemic lesions noted were as follows: nodules in the lungs, cases 1, 3, 5 and 8; fibrocystic disease of the bones, cases 1, 2 and 3; splenomegaly, cases 1, 3, 7 and 8; adenopathy, cases 1 and 7; atrophic rhinitis, case 1; chronic parotitis, cases 5 and 7; iritis, case 2, and jaundice, cases 7 and 8.

There was no evidence in this series that the cases with associated systemic lesions represented a disease different from those in which only lesions of the skin were demonstrable. The cases in which the lupus pernio type of eruption was present were associated with various systemic lesions with the exception possibly of case 4. The fibrocystic changes in bone evidently are monopolized by this group. It must be borne in mind, however, that the group is small and that such a condition would not necessarily lend much weight to the assumption that such cases may represent a disease sui generis. As might be suspected, the patients with systemic lesions were more likely to have poor general health and many complaints. This was particularly true of cases 5, 7 and 8. The jaundice reported in cases 7 and 8 was unique and will bear further observation. It may have been incidental in the sense that there may have been some disturbance in the gallbladder or biliary tract entirely apart from the factor producing the lesions of the skin, and other lesions. I am inclined to believe, however, that the jaundice was part of the syndrome, possibly resulting from the pressure of enlarged nodes on the biliary ducts. This could be determined definitely only by operation or necropsy.

ETIOLOGY

The evidence favoring tuberculosis as a cause of sarcoids and related lesions has been consistently increasing and probably has the most adher-

24. Bloch, B.: Lupus pernio bei 39 jähriger Frau mit Tuberkulöse-Belastung. Cor.-Bl. f. schweiz. Aerzte. **58**:1254, 1918

25. Jüngling, Otto: Ostitis Tuberculosa multiplex Cystica (eine eigenartige Form der Knochentuberkulose), Fortschr. a. d. Geb. d. Röntgenstrahlen **27**: 375, 1919-1920.

26. Gans, Oscar: Ueber Lupus pernio und seine Beziehungen zum Sarkoid Boeck, Dermat. Ztschr. **33**:64, 1921; Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, pp. 621.

ents at the present time. The tuberculous nature of typical cases of erythema induratum is universally conceded. Foerster, Stokes and others have shown that typical cases of erythema nodosum may be due to tuberculosis. Wende has demonstrated positively that his case, so closely resembling Boeck's sarcoid, resulted from tuberculosis. If the bacillus of tuberculosis can be demonstrated definitely as the etiologic agent in sarcoid and lupus pernio, the close relationship of all these lesions is easily conceivable, and will explain the lack of sharply defined clinical pictures in so many of these cases. Kyrle demonstrated the bacillus in a section taken from early lesions in a case of Boeck's sarcoid. Ruete [27] was also able to demonstrate an acid-fast bacillus in a section taken from a case of Boeck's sarcoid. Gans demonstrated the organism by guinea-pig inoculation with a piece of tissue removed in a case of lupus pernio. The demonstration of bacilli is probably the most positive evidence of the tuberculous origin of these lesions. Other observations contribute further suggestive evidence. In 1914, Sweitzer reported a case of sarcoid in which guinea-pig inoculation produced nodules suggesting tuberculosis, and expressed the belief that at least some of the sarcoids are tuberculous in character. In 1919, Sweitzer and Michelson, reported a case in which they were struck by the close resemblance of the histologic structure of the lesions to erythema induratum, which is admittedly tuberculous in nature. Jüngling contributed to this phase of the study by careful investigation of the fibrocystic changes of the bone in several cases of lupus pernio. Schaumann, who made a detailed investigation, also favors the theory of a tuberculous cause, and even goes so far as to incriminate the bovine strain, thus explaining the peculiar reaction of the organism in producing the sarcoid lesions.

Other observers have not accepted the foregoing cause. Rischin argued, with Kuznitzky and Bittorf, that the sarcoids with internal lesions represent a disease sui generis. Whitmore [28] reported a case of type 3 sarcoid, which now would probably be called erythema induratum, in which he established sepsis as the probable etiologic factor. This case will, however, have to be interpreted with considerable caution; there is no doubt, as Zeisler and others have pointed out, that other etiologic agents may produce a clinical picture closely resembling the sarcoids. Possibly it will be necessary to classify this case with those reported by Pfeifer, Kraus and others. The school that contends against the tuberculous nature of the sarcoids bases its arguments chiefly on the facts that the tuberculin test is usually negative, that bacilli of tuber-

27. Ruete, A.: Zur Aetiologie der Boeckschen Erkrankung, Dermat. Ztschr. **37**:129, 1922-1923.

28. Whitmore, E. R.: Type III Sarcoid Associated with Infection of Tonsils and Gums, Arch. Dermat. & Syph. **11**:56 (Jan.) 1925.

culosis can practically never be demonstrated in the tissue by the microscope, and that inoculation of guinea-pigs with sarcoidal tissue will not produce tuberculosis in the animal. A priori it would seem that such arguments are difficult to confute and much careful work has been done to invalidate them. Jadassohn, a champion of tuberculosis as a cause, has long explained the negative tuberculin test in these cases as due to true anergy, essentially a state of absolute immunity. Martenstein,[29] after careful serologic studies, came to a similar conclusion. Sahli [30] readily admitted the possibility of a negative tuberculin reaction as the result of gradual development of complete immunity. Kyrle attributed the difficulty of demonstrating the bacillus of tuberculosis in sections and by inoculation to the fact that the bacillus is of low virulence and the allergy in such cases rather high. In essence, the bacilli die promptly when they have reached the site where the lesion appears. The so-called sarcoid, according to Kyrle, is actually a rather distinct type of foreign body reaction to the bacillus of tuberculosis and its disintegration products. He reached this conclusion from observations made on a case in which the earliest lesions showed numerous bacilli. Shortly afterward, only a few bacilli could be found, and later it was impossible to find any, although the lesions had taken on the typical appearance of sarcoids. This conception finds support in Lewandowsky's careful experimental work; he showed that the subcutaneously injected living bacilli could not be found in a partially immunized animal after a short time, although the local lesions might persist for months. The bacillus of tuberculosis is not unique in this respect. *Spirochaeta pallida* behaves similarly in tissue possessing the proper allergy. It is a familiar fact that the organism can be found only with the greatest difficulty in the late syphilids, while it is present in large numbers in the early lesions. That the immunity reaction is unusually pronounced in these cases is further evidenced by the fact that the tuberculin test is practically always negative in contrast to the fact that reaction occurs in from 60 to 70 per cent of seemingly healthy persons.

If one accepts the avirulent or dead bacilli of tuberculosis, given the proper soil, as the cause of the sarcoids, one has a plausible explanation for both the fairly typical characteristics or at times the close similarity of the sarcoids to other foreign body reactions. Kyrle explained this by assuming a definite biologic tissue allergy, and that the skin has an inherent ability reinforced by an acquired ability to react to various foreign substances by the formation of tuberculoid granuloma.

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29. Martenstein, Hans: Sarkoid Boeck und Lupus pernio, Arch. f. Dermat. u. Syph. **147**:70, 1924.

30. Sahli, H.: Ueber Tuberkulinbehandlung mit besonderer Berücksichtigung der Intrakulenbehandlung, Schweiz. med. Wchnschr. **50**:557 (July) 1920.

If bacilli enter the skin in large numbers and proliferate actively, the skin answers with a banal inflammatory and not with a tuberculoid reaction; but when bacilli are inactive, they produce a tuberculoid structure. There is, to be sure, a preliminary stage showing a banal inflammatory reaction preceding the tuberculoid structure and this may vary markedly both in intensity and duration. These facts are strikingly illustrated by the various stages in the development of the sarcoids, as well as by certain lesions of syphilis and leprosy, when the early lesions show ordinary inflammatory reaction, gradually developing a mixture of giant cells which later decrease in number as the infiltration assumes the structure of an almost pure epithelioid cell granuloma. The giant cell speaks for the presence of micro-organisms or their decomposition products. When the giant cells grow less in number, it is a sign that most of the offending organisms have been eliminated. Should only epithelioid cells be found, it is a sign that the focus is entirely free from micro-organisms. This conception of the pathologic physiology of a sarcoid's development readily explains also why the bacilli of tuberculosis are demonstrable in these lesions for only a limited period during the early part of their development, as the bacilli probably begin to disintegrate about the time the first features of the tuberculoid reaction appear. Possibly the experimental work of Morse and Stott [31] on reactions of tissue to various products of the bacillus affords a more tangible explanation. It has usually been assumed that the histologic lesion caused by the bacillus was due to a toxin liberated from the body of the bacillus by action of the tissue cells. These observers show that a boiling alcohol extract yields a waxlike substance that produces lesions microscopically identical with those produced by the whole dead bacillus. There was never any caseation. They did not determine whether the wax is a single substance or a mixture of several substances. It may be that these observations will explain the difficulty encountered at times in distinguishing microscopically tuberculous lesions from foreign body reactions, especially those due to various oils. If this waxy substance alone is able to produce the tuberculoid lesions, it is easy to see why these lesions may persist essentially as foreign body tumors for such a long time in the absence of actual bacilli. The isolation of a protein and a phosphatide from the bacillus of tuberculosis by Anderson,[32] and Sabin and Doan,[33] and their demonstration of a

31. Morse, P. F., and Stott, Ethel: Studies of the Tissue Reactions to Various Products of the Tubercle Bacillus, J. Lab. & Clin. Med. **2**:159 (Dec.) 1916.

32. Anderson, R. J.: The Separation of Lipoid Fractions from Tubercle Bacilli, J. Biol. Chem. **74**:525 (Sept.) 1927.

33. Sabin, Florence R., and Doan, C. A.: The Biological Reaction in Rabbits to the Protein and Phosphatide Fractions from the Chemical Analysis of Human Tubercle Bacilli, J. Exper. Med. **46**:645 (Oct.) 1927.

specific cellular reaction to either may further help to explain the peculiar behavior of the sarcoids.

Kyrle is undoubtedly right in emphasizing the importance of the positive demonstrations of the bacillus of tuberculosis as contrasted with the numerous negative results. The practical lessons to be drawn from his observations are not to excise a piece of tissue from a classical lesion for demonstration of the bacillus by staining or by animal inoculation, but to obtain the earliest lesion for this purpose. I am fully aware that the demonstration of the bacillus in a lesion in one or two instances does not conclusively demonstrate its etiology, but the facts recorded by Kyrle would seem sufficient to warrant an intensive effort to demonstrate the bacillus in tissue by staining as well as by animal inoculation in the earliest lesions. Although some of the cases reported have been carefully studied from the standpoint of histology and animal inoculation, it has not thus far been possible to demonstrate the bacillus of tuberculosis. I must emphasize the fact, however, that I believe such studies were not made properly, in the light of the observations recorded here. In the cases seen years ago, the microscopic changes were studied in an endeavor to demonstrate the classic morphology, and an attempt was not made to demonstrate the bacillus. When it was attempted in others, a fairly classic lesion was excised for examination, a procedure which is now known to be usually doomed to failure. In a few cases, an effort was made to obtain the latest lesion both for staining for the bacillus and for animal inoculation. The cases, however, were not especially suitable for such study because even the latest lesions had been present for some time. It is likely that demonstration of bacilli is possible only in exceptional cases. Clinical observations are probably of less value in an effort to establish the tuberculous cause of the sarcoids. The general condition of the patient and the presence or absence of other forms of tuberculosis would only be of relative value. In cases of lupus vulgaris or papulonecrotic tuberculides, it is not uncommon to see unusually robust persons with no other demonstrable evidence of tuberculosis. This holds also for the sarcoids. Yet it is difficult to deny the possibility of a tuberculous cause of a lesion when other evidence of tuberculosis is frequently associated with it. There are a number of such reports in the literature but I could find nothing that would carry conviction on a possible etiologic relationship. A review of the cases in this series with reference to the presence of other clinical evidence of tuberculosis is of some importance because all the cases were studied for collateral evidence of this disease. Definite evidence of the infection either in the lungs or elsewhere was found in cases 3, 11, 12, 13, 14 and 15. It will be noted that most of the cases appeared in the group which presented a fairly typical type of Boeck's sarcoid. Only in case 3 was there definite evidence of tuberculosis in the type

that might be called lupus pernio, and there was no evidence of tuberculosis in any of those that I should like to regard as atypical. Conclusions cannot be drawn, as tuberculosis might have been demonstrable in an equal number of unselected cases. The fact that five of seven cases (70 per cent) of the Boeck type showed tuberculosis while it could be demonstrated in only one of the others, does not seem entirely negligible. The possibility of differences in the immunity reaction as explanatory of the variations in the cutaneous picture is suggested. There is no doubt of the existence of such variations even if it is assumed that all these lesions are due to invasion by the bacillus of tuberculosis. Further speculation on this point is probably futile, however, until it has been conclusively proved that the bacillus of tuberculosis is the only cause of sarcoids and related lesions. Case 3 of this series with its active lesions in the pharynx and larynx, speaks against the outright assumption of a high degree of allergy throughout, but does not necessarily invalidate the assumption of an allergic reaction as a factor in the production of sarcoids. It is possible that certain tissues may possess this allergy to a greater degree than others, which would help to explain why the nodular lesions are essentially found in the skin, the lungs, lymphatic and splenic tissues and possibly the bones.

On the assumption that sarcoids are essentially a peculiar foreign body reaction to the dead bacillus of tuberculosis in cases of marked allergic reactions, in association with Dr. Rubinstein, I endeavored to produce sarcoids experimentally in animals. Baldwin,[34] Petroff,[35] and others have shown that hypersensitiveness of skin can be produced by repeated inoculations with dead bacilli. Accordingly, we endeavored to sensitize guinea-pigs and then injected dead bacilli intracutaneously. A detailed report of this work will form the subject of a separate communication.

MICROSCOPIC CHANGES

When Boeck first described the sarcoids, he stated that the histologic appearance of the lesion was unique. This statement can no longer be upheld. In a fully developed lesion it is probably true, but in the earlier stages the picture is nonspecific, such as may be seen in any type of chronic inflammatory reaction. Kyrle has shown that in the early lesions the cellular infiltrate is confined to the dilated vessels of the papillae and the cutis. The infiltrate consists chiefly of lymphocytes, although even at this time certain proliferating connective tissue cells and epithelioid cells are present in small numbers. The lesion then gradually assumes the characteristic picture. It is particularly during

34. Baldwin, E. R., quoted by Petroff: Immunity in Tuberculosis Vaccination with Living Virulent Avirulent and Dead Tubercle Bacilli, J. A. M. A. **89**:285 (July 23) 1927.

35. Petroff, S. A.: J. A. M. A. **89**:285 (July 23) 1927.

the earlier stages that the data do not permit of a differential diagnosis from erythema induratum. Wende's description of the microscopic changes in the case he reported would also fit admirably the description of an early sarcoid. It is, however, practically impossible to distinguish Boeck's sarcoid from lupus pernio by histologic study at any time during the development of the lesion, so closely do they resemble each other. The difficulty of differentiating, microscopically, this entire group is particularly emphasized also by Gans, Martenstein and Schaumann. The cases reported in my series bear this out. Sections were obtained from twelve of the seventeen cases. Of these twelve, nine showed the typical microscopic picture of Boeck's sarcoid; two of these were clinically lupus pernio (cases 1 and 2). One case (case 5) was typical microscopically of sarcoid but was clinically on the borderline between sarcoid and lupus pernio. One case (case 8) was typical microscopically of Boeck's sarcoid. Clinically, the lesions also were characteristic, but there were associated systemic lesions in the form of marked infiltration of the lungs, splenomegaly and jaundice. Despite the associated systemic lesions, the typical clinical and histologic features would hardly justify the assumption of a disease sui generis, but would rather favor the identity of such cases with sarcoids. Case 6 was atypical microscopically but rather typical clinically. The disease was of a rather acute type which may explain the absence of typical epithelioid tubercles. Case 9 was atypical clinically because of the distribution of the lesions on the soles, however, the histologic lesion was typical. This case probably corresponds to those reported by Jadassohn and Kuznitzky. Case 12 showed a rather typical clinical lesion, but the histologic section was atypical. In this case, the atypical appearance could not be explained by the acuteness of the lesion, since it had been present for five years. It is possible that a piece of material may have been obtained from the periphery of the lesion resulting from recent hematogenous infiltration. According to Kyrle, some sarcoids spread peripherally in this manner. Case 14 was rather typical clinically but atypical histologically. Cases 11, 13, 16 and 17 were rather classic cases of sarcoids of the Boeck type both clinically and microscopically.

TREATMENT

For a long time arsenic has been considered a specific for Boeck's sarcoid. Certain observers still hold that the lesions will usually respond to this drug and that the diagnosis is doubtful if they do not, an opinion hardly tenable today. The cases in this series did not invariably respond to arsenic. Arsenic was given to eight of the seventeen patients either in the form of solution of potassium arsenite, Asiatic pills or neoarsphenamine. There was slight improvement in five and none in three. In only two did the lesions disappear entirely. In one

of the cases in which improvement was not noted the condition was a classic Boeck's sarcoid; the other two could better be classified with lupus pernio. It would seem, therefore, that arsenic cannot be used as a therapeutic test, as some of the lesions improve and others do not. Other therapeutic measures that have been employed with some degree of success are tuberculin, ultraviolet light and carbon dioxide snow; the latter seems especially worthy of further trial.

SUMMARY

There is a group of nodular lesions so closely related in their clinical and histologic manifestations that a sharp dividing line cannot be drawn. This group includes the cutaneous lesions commonly referred to as Boeck's and Darier-Roussy sarcoids, lupus pernio, erythema induratum, and probably Wende's nodular tuberculosis of the hypoderm. The lesions are probably produced by the bacillus of tuberculosis. Clinically, other cases simulating these are seen, but histologically, they usually are sufficiently different to warrant distinction. Such cases apparently are chiefly encountered in various chronic infections and in cachetic conditions. Lesions occasionally seen in syphilis, leprosy or the lymphoblastomas, and other conditions, just because they may resemble the sarcoids clinically or even microscopically, should not be classified with sarcoids. Their fundamental difference will usually become apparent by careful study and prolonged observation of their behavior. The cases reported in this paper illustrate in a measure the impossibility of drawing a sharp dividing line between the so-called sarcoids and the related lesions. This entire group may sometimes be associated with characteristic lesions in other structures, which will help to separate the cases from those that do not belong in this group. The associated lesions are commonly seen as infiltrations in the finer bronchioles and fibrocystic changes of the bone. It is likely that the splenomegaly often noticed is the result of infiltrations similar to those seen in the skin. The other symptoms, for example, adenopathy, iritis, parotitis and atrophic rhinitis, are seen in so many chronic diseases that they may be considered of less importance, but when present may be looked on as part of the entire syndrome. There are at present three distinct hypotheses as to the etiology of these lesions; the one favoring tuberculosis has the most adherents. Supporters of the second hypothesis regard the lesions as representative of a disease sui generis, and those of the third hypothesis believe that the etiology may be varied. A careful review of the literature and my own observations influence me to favor the first view. The microscopic changes in the lesions do not afford a definite clue as to the etiology, but they do not present any features that are not compatible with tuberculosis. In fact, good general pathologists have, in my experience, repeatedly and unhesi-

tatingly made the diagnosis of tuberculosis on the basis of sections for microscopic examination submitted from a number of cases reported. There is nothing in microscopic changes in a given case that would permit of sharp differentiation. Arsenic is not invariably successful in eliminating a classic Boeck's sarcoid. Again, the lesions may involute promptly when the drug is given. This holds true also to a lesser degree in the transitional cases. I have not observed improvement in the lupus pernio type. Arsenic can probably not be used as a therapeutic test to differentiate these lesions, or those simulating them in other diseases.

CONCLUSIONS

1. Sharp differentiation in all cases of Boeck's and Darier-Roussy sarcoids, lupus pernio, erythema induratum and nodular tuberculosis of the hypoderm is practically impossible.

2. This group of lesions is probably the result of invasion by the bacillus of tuberculosis.

3. Other lesions that simulate this group closely can usually be differentiated by careful study and prolonged observation.

4. Lesions in other tissues often associated with lesions of this group should be recognized as part of a syndrome of which sarcoids, lupus pernio, erythema induratum and similar infections are only the cutaneous manifestations.

5. Such associated lesions may help to classify properly the cutaneous lesions and vice versa.

6. The microscopic changes are not sufficiently specific to use as an aid in differentiating the lesions. They may even fail to help in distinguishing them from certain cutaneous lesions of syphilis, leprosy and other established disease entities.

7. Arsenic is not a specific in Boeck's sarcoid nor in any of the related lesions.

STANDARDIZATION OF THE TRYPANOCIDAL TEST AND OF THE TRYPANOCIDAL VALUE OF ARSPHENAMINE

BASED ON MORE THAN ONE HUNDRED TESTS

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PHILADELPHIA

The therapeutic value of arsphenamine was established by Ehrlich and Hata [1] as a result of experiments on various animals (mice, rats, chickens and rabbits) inoculated with syphilis, trypanosomiasis, chicken spirillosis and recurrent fever. The nature of these diseases is such as to permit of a more or less direct observation of the effect of the drug on the causative agent. Recurrent fever and chicken spirillosis are both blood infections, and systematic examination of the blood affords a fair picture of the effect of the drug on the organisms. As for experimental syphilis, conclusions may be drawn from the disappearance of spirochetes from the chancre and the healing of the lesions.

An unfavorable feature of this test for the spirocheticidal activity of drugs, as originally employed by Ehrlich and Hata, is that animals infected with chicken spirillosis, relapsing fever and, to some extent, with syphilis may recover spontaneously. On this account, cures cannot be attributed solely to the drug, and therefore conclusions as to the curative effect of the tested drug must be drawn from comparisons between the course of the disease in treated and in nontreated (control) animals. In addition, syphilis takes a slow course in the rabbit, the animal best suited for experimental syphilis, thereby rendering such experimentation long and expensive. These factors made it desirable to employ trypanosomes in the investigation of the curative effect of drugs, since the experiments of Ehrlich proved that arsphenamine is effective in experimental trypanosomiasis in small animals. The advantage of the use of this infection is that it usually assumes an acute course in mice and white rats, generally resulting in the death of the animal. Thus the slightest curative effect of the drug can be definitely ascertained. Many species of trypanosomes were found

1. Ehrlich and Hata: The Experimental Chemotherapy of Spirilloses, London, 1911.

suitable for these experiments by various investigators, e.g., *Trypanosoma lewisi* (a nonpathogenic parasite found in the blood of rats), *Trypanosoma brucei* (the parasite of nagana), *Trypanosoma evansi* (the parasite of surra), and other parasitic forms. In 1920, Schamberg, Kolmer and Raiziss [2] suggested the use of *Trypanosoma equiperdum* (the parasite of dourine) in preference to the parasitic organisms already mentioned, because the results with this strain are sharper and more decisive than those observed with the relatively nonvirulent *Trypanosoma lewisi* and also better than with *Trypanosoma brucei*, which is too virulent and kills the animal too quickly. For the past six years, *Trypanosoma equiperdum* has been used by many investigators in the standard tests with arsphenamine.

Although a suitable organism for testing arsphenamine was thus found and the possibility of spontaneous cure was eliminated, the method still lacked exactness. This was considered an objectionable feature by chemotherapeutists. Ehrlich and Hata had observed that the number of micro-organisms in the inoculum has a bearing on the number of organisms appearing in the blood of the infected animal and the virulence of the disease. The same was latter proved by Schamberg, Kolmer and Raiziss with relation to experimental trypanosomiasis.[3] Since the curative effect of a drug is dependent on the severity of the infection, the latter must be taken into consideration in the evaluation of therapeutic efficiency. Therefore, Ehrlich and Hata distinguished between a heavy, moderate and slight infection, according to the approximate number of parasites in the inoculum and in the infected body. In 1915,[4] Kolmer suggested a method for the exact measurement of the strength of the inoculum and also of the infection. Briefly, the method consists in first determining the number of trypanosomes in a cubic centimeter of the blood of a seed animal (by examining a definite volume in the counting chamber under the microscope) and preparing an inoculum of definite strength by so diluting the total volume of blood taken for injection that it will contain the desired number of organisms per rat. In 1917, Kolmer, Schamberg and Raiziss [3] by this method inoculated rats with known numbers of *Trypanosoma equiperdum* and studied the effects produced by various doses of arsphenamine.

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2. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: A Comparative Study of the Trypanocidal Activity of Arsphenamine and Neoarsphenamine, Am. J. M. Sc. **160**:25, 1920.

3. Kolmer, J. A.; Schamberg, J. F., and Raiziss, G. W.: The Numeric Relationship of Infection to the Chemotherapy of Experimental Trypanosomiasis, J. Infect. Dis. **20**:10 and 35 (Jan.) 1917.

4. Kolmer: A Method of Transmitting Known Numbers of Trypanosomes, J. Infect. Dis. **17**:79, 1915.

In 1922, Voegtlin and Miller [5] further standardized the method for comparing the trypanocidal power of drugs and also introduced new and valuable modifications. The principle of their procedure consists in determining the minimum amount of a drug required to sterilize, in twenty-four hours, white rats infected with a uniformly definite number of parasites. Rats weighing between 100 and 150 Gm. are infected with an inoculum which in twenty-four hours will produce from 100,000 to 250,000 parasites per cubic millimeter, preferably 100,000 to 150,000. The drug is administered twenty-four hours after the infection. Prior to the injection of the drug, however, the number of the trypanosomes in the peripheral blood is verified. If it is less than 100,000, treatment is delayed until later in the day, when the required stage of infection is attained (the number of parasites doubles in about seven hours). Twenty-four hours after the administration of the drug, the blood is examined for trypanosomes; this is repeated every twenty-four hours for three days. The dose required to reduce the parasitic count to a trace or zero within twenty-four to seventy-two hours or, in other words, the dose which will destroy from 100,000 to 250,000 parasites per cubic millimeter in twenty-four to seventy-two hours, is called the minimum effective dose, and the value of the various preparations is gaged by the size of this dose. The method that has been described renders possible a more or less exact comparison of the trypanocidal power of drugs tested at various times by different experimenters; in other words, it supplies chemotherapeutists with a common measure. To secure even greater accuracy, since the resistance of the trypanosomes may fluctuate, it was decided at the International Conference on Biological Standardization [6] held at Geneva in 1926 under the auspices of the League of Nations to make the trypanocidal test a comparative one. For each test two groups of animals should be infected with the same inoculum. One group should then be treated with the drug under consideration, the other with a standard product, and the results of both compared. The tested drug should exhibit a therapeutic efficiency at least as great as the standard.

AUTHORS' EXPERIMENTAL WORK

Since 1923, we have employed in our laboratories both Voegtlin and Miller's method and the comparative principle for testing the parasiticidal power of arsphenamine. As a standard, we used a selected amount of arsphenamine prepared by us in 1922 and preserved in vacuum ampules. Between 1923 and 1926, we performed over 100 such tests, in each of

5. Voegtlin, C., and Miller, D. W.: The Relative Parasiticidal Value of Arsphenamine and Neoarsphenamine, Pub. Health Rep. **37**:1627 (July 7) 1922.

6. Second International Conference on the Biological Standardization of Certain Remedies, Pub. Health Rep., March 19, 1926, p. 505.

which the standard arsphenamine and the strain of *Trypanosoma equiperdum* were the same. The latter was transmitted by us through many generations of white rats.

We introduced a modification in the method recommended by Voegtlin and Miller, which, in our opinion, increased the exactness of the test. Thus, in addition to reading the results, twenty-four, forty-eight and seventy-two hours after injection of the drug, as suggested in the original procedure, we examined the blood of the animals daily for twenty-one days. We were prompted to this course by the observations of Schamberg, Kolmer and Raiziss [2] and others that the disappearance of trypanosomes from the circulation in the first few days does not prove actual sterilization of the animal, as the organisms may subsequently be found again in the blood. This can be seen from the following table, in which are summarized the results of our tests made in the course of

TABLE 1.—*Trypanocidal Tests with a Standard Sample of Arsphenamine (in White Rats)*

Dose per Kilogram of Body Weight	Number of Individual Tests	Blood Observations After 72 Hours			Blood Observations After 21 Days		
		Negative	Positive	Percentage of Negative Observations	Negative	Positive	Percentage of Negative Observations
0.002 Gm.	66	8	58	12	3	63	4.5
0.004 Gm.	76	66	10	87	23	53	30
0.006 Gm.	33	32	1	97	23	10	70

TABLE 2.—*Relationship Between Dosage and Pseudosterilization*

Dosage per Kilogram	Number of Negative Observations After 72 Hours	Number of Negative Cases which Turned Positive Later	Percentage of Pseudo Sterilization in the Cases Negative After 72 Hours
0.002 Gm.	8	8	100
0.004 Gm.	66	43	65
0.006 Gm.	32	9	28

about three years with the same standard sample of arsphenamine. The readings, made seventy-two hours and twenty-one days after treatment, are given in table 1.

From the observations in table 1, it is evident that the reading of results after seventy-two hours may be misleading. This is particularly striking in those instances in which the dose of 0.004 Gm. of arsphenamine was administered. From a total of seventy-six tests, sterilization was apparently achieved in sixty-six, judging from the observations after seventy-two hours. Subsequent examinations, however, showed that only twenty-three animals were sterilized.

The percentage of cases of pseudosterilization is inversely proportional to the size of the dosage, i.e., the larger the dose, the smaller the percentage. This can be readily observed in table 2.

All of the eight cases of this group which were negative in seventy-two hours became positive later. It is interesting to note, however, that three of the fifty-eight positive cases (table 1) later became negative, so that instead of sixty-six positive observations after twenty-one days there were only sixty-three.

The divergency of the results may be explained as follows: When the number of trypanosomes becomes comparatively small on account of the action of the drug, organisms may not be present in the drop of blood taken for the test, yet many of them may survive elsewhere. With the passage of time, these remaining organisms multiply and appear again in large numbers in the blood stream.

This fact has a great bearing on the value of the trypanocidal test as usually performed, both with regard to the determination of the relative potency of a drug and the establishment of the minimum therapeutic dose. In a three days' test, a drug may show the same potency as, for example, 0.004 Gm. of arsphenamine, yet, actually, it may be much more efficacious and clear up the infection entirely—a result not often obtained with 0.004 Gm. of arsphenamine. On the other hand, it may prove less effective than the standard drug in a prolonged test. We have often encountered such cases in our experiments. Again, a three days' test does not yield true figures for the minimum therapeutic dose of a drug. Thus, according to the results obtained under the foregoing condition, 0.004 Gm. of arsphenamine per kilogram of body weight may be considered as the minimum therapeutic dose for rats infected according to the Voegtlin and Miller method, since this quantity effects sterilization in 87 per cent of cases. The 13 per cent of failures may be largely ascribed to individual conditions. Prolonged observation, however, discloses the fact that the percentage of failures with the same dose of arsphenamine is 70 per cent, thereby affording convincing proof that the 0.004 Gm. dose is decidedly nonsterilizing.

Our data seem to indicate that even 0.006 Gm. of arsphenamine cannot be considered a definitely sterilizing dose, since it did not exterminate the infection in thirty per cent of our cases. A sterilizing dose of 0.008 Gm. may be safely regarded as the minimum.

In carrying out the trypanocidal test, the use of an unusually resistant strain of the micro-organisms must be guarded against. This can be determined in advance by injecting into several control animals the minimum therapeutic dose of a known sample of the drug and observing them for twenty-one days. If sterilization is effected in a majority of the controls, it can be safely assumed that the strain of trypanosomes is normal. We have found that a strain of *Trypanosoma equiperdum* which has become unusually resistant can be reduced to normal (average) resistance by one or several passages through rabbits.

In order to preclude the possibility of using too weak a strain of trypanosomes, we first inject several control animals with a dose smaller than the minimum therapeutic dose, e.g., 0.002 Gm. of arsphenamine. If a large number of animals survive, it is conclusive evidence that the particular strain of micro-organisms is not sufficiently drug-resistant for the regular trypanocidal test. In testing the virulence of trypanosomes, definite results can be obtained only when arsphenamine of known potency, such as our standard arsphenamine, is used in all of the experiments.

A review of all of our trypanocidal tests discloses the possibility of ultimately standardizing a test for the accurate and quantitative estimation of the therapeutic value of arsphenamine or other organic compounds of arsenic. In our tests, we employed the same lot of arsphenamine for three consecutive years. This product, in a dosage of 0.006 Gm. per kilogram of body weight, in most cases sterilized uniformly infected albino rats. The resistance of *Trypanosoma equiperdum*

TABLE 3.—*Therapeutic Effect in Trypanosomiasis*

Chemical Compound	Dose Gm. per Kg.	Days After Injection											
		1	2	3	4	5	6	7	8	9	10	11	12 to 21
Arsphenamine, No. 47825 (index)	0.002	+2	+4	D									
	0.004	—	—	—	—	—	—	—	—	±	+4	D	
	0.006	—	—	—	—	—	—	—	—	—	—	—	—
No. 411 3-amino-4-chloro acetylarsanilic acid	0.080	+4	D										
	0.160	+4	D										
No. 930 N(phenyl-4-arsonic acid) glycine-4'-aminoguaiacol	0.080	—	few	+4	+4	D							
	0.160	—	—	few	—	—	±	1+	2+	4+	D		

to the drug can be maintained at the same level by passing the organisms from one rat to another at certain intervals—in our case about a week. When the resistance of a strain of micro-organisms becomes too great, passage through a rabbit serves to reduce it to normal. The sensitiveness of this test is evident from the fact that 0.004 Gm. of arsphenamine fails to sterilize experimental animals while 0.006 Gm. invariably does so.

In order to obtain strictly quantitative and comparative results, the method of determining trypanocidal value as described by Voegtlin and Miller must be followed in every detail. In addition, we found it more satisfactory to use rats the blood of which contained from 100,000 to 150,000 trypanosomes per cubic millimeter, with the latter number as a maximum. Too high as well as too low a trypanosome content of the blood is undesirable. The intravenous injections of the chemical compounds must be made with great accuracy. A definite solution of the drug is prepared immediately before the animals are ready to be given injections. The subdilutions for graded doses are made with sterile, distilled water which is measured in accurately graduated pipets. A quantity of standard arsphenamine sufficient to last for many years can

be preserved in vacuum ampules. Table 3 shows the results of one of the tests performed by us according to the standard procedure.

Table 3 represents results obtained by us in our usual routine tests. As seen in the table, the blood was examined for the presence of trypanosomes for twenty-one days. At the end of seventy-two hours, complete disappearance of trypanosomes from the blood was effected in animals treated with 4 and 6 mg. of arsphenamine per kilogram of body weight. However, the animal that received 4 mg. per kilogram showed a reappearance of trypanosomes on the ninth day; death, due to the infection, occurred on the eleventh day. On the contrary, the animal treated with 6 mg. per kilogram remained free of trypanosomes for twenty-one days. Thus, it is evident that the reading at the end of seventy-two hours is not as accurate as that at the end of twenty-one days.

Preparation 411, a pentavalent arsenical, is not effective in doses of 80 and even 160 mg. per kilogram. The value of this method for the quick appraisal of a product is readily apparent. In a course of a few days, one can see that this particular product is a comparatively weak trypanocide and cannot be compared with the powerful trivalent arsenical, arsphenamine.

Product 930[7] is inefficient in a dose of 80 mg. per kilogram after the expiration of seventy-two hours. If only the reading at this time were taken into consideration, it would appear that 160 mg. is the minimum therapeutic dose. Further observations, however, indicate that this is not the case; at the end of six days trypanosomes reappeared, and these increased in numbers until the tenth day, when the animal died on account of the infection.

CONCLUSIONS

1. *Trypanosoma equiperdum* (the parasite of dourine) is exceptionally valuable in the quantitative determination of the minimum therapeutic dose of organic compounds of arsenic. This was first suggested in 1920 by Schamberg, Kolmer and Raiziss.

2. This quantitative test is based on the method of infecting albino rats with known numbers of trypanosomes according to a procedure outlined by Kolmer, Schamberg and Raiziss in 1917. The standardization of the degree of infection is a basic requirement for a quantitative test.

3. The standardization of the infection was further improved by Voegtlin and Miller in 1922, when they proposed to employ for the test rats carrying only a definite number of parasites, namely, 100,000 to 250,000 per cubic millimeter of peripheral blood.

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7. A new organic compound of arsenic prepared by Raiziss and Fisher in the course of chemotherapeutic research.

4. The trypanocidal test, as described by Voegtlin and Miller, is valuable and yields good results for the quantitative estimation of the minimum therapeutic dose if the final readings are made at the end of at least twenty-one days, as proposed by us.

5. One hundred consecutive tests performed by us in the course of three years indicate that the reading of results at the end of from forty-eight to seventy-two hours according to the technic of Voegtlin and Miller may cause an overestimation of the therapeutic value of drugs.

6. The trypanocidal test, in addition to the usual regulation of the virulence of trypanosomes, requires also the use of a standard chemical compound as a further check on the resistance of the parasites.

7. Arsphenamine is best adapted for this purpose.

8. From the results of our 100 tests carried out according to the standard method, we believe that arsphenamine of definite therapeutic quality should sterilize rats infected with *Trypanosoma equiperdum* in a dose of 0.006 to 0.008 Gm. per kilogram by the intravenous route.

MYCOTIC INGUINAL LYMPHADENITIS ASSOCIATED WITH SUPERFICIAL FUNGUS DERMATITIS OF THE FEET

II. STUDIES IN MYCOTIC DERMATITIS *

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An acute exacerbation of superficial mycotic dermatitis of the feet is occasionally accompanied by regional inguinal lymphadenopathy. Often there are systemic manifestations, such as a moderate degree of fever, and some malaise; these constitutional symptoms are rarely, if at all, mentioned in the standard dermatologic textbooks. The primary focus of infection is situated in one or more of the intertriginous areas of the toes, especially in the third or fourth. In a clinical and laboratory study of superficial mycotic dermatitis in 648 patients made by me practically all of the patients showed pedal interdigital foci; seven presented varying degrees of inguinal adenopathy, usually unilateral, together with a flare-up of the feet lesions. Of these, three had some fever and mild constitutional symptoms. Another patient exhibited unilateral axillary adenopathy secondary to an acute eruption on the fingers.

The paramount issue was to determine whether such inguinal lymphadenitis was pyogenic, mycotoxic or actually mycotic. Recently, a thorough investigation was carried out on one such patient and resulted in the recovery of the offending fungus from an inguinal lymph node and the primary pedal lesions, both microscopically and culturally from each area. Because of the paucity of reports of such positive observations in the world's literature, and because of a possible bearing on the endogenous method of dissemination of fungi in man, this case is reported.

REPORT OF A CASE

History.—E. S., aged 20, a gardener, was admitted on July 17, 1927, to the observation wards of the Buffalo City Hospital on account of possible iodine poisoning, the drug having been taken with suicidal intent. Emesis occurred soon after ingestion, and on admittance no clinical or laboratory evidence could be elicited to detect iodine intoxication. At his entrance examination, he was found to have bilateral inguinal buboes, which were tender and discrete and approximated the size of a walnut with the right side slightly larger than

* Drs. Richard Saunders and G. Warren Hyde of the resident staff of the Buffalo City Hospital aided materially in the study of the patient.

the left; the overlying skin was normal. The genitalia were normal; other evidences of adenopathy could not be found. The results of the rest of the general examination were negative except for a patchy erythematosquamous eruption on the feet. He gave a history of several of the childhood exanthems. Coincident with a gonorrheal infection in 1925, he had had a penile chancre; he had been treated for both of these conditions in the U. S. Navy. Because of the pronounced inguinal bubo, the opinion of the urologic department was sought; they did not discover any evidence of urethral discharge, chancroid or other penile lesions. Their further inquiry revealed the enlarged lymph nodes to be of two weeks' duration and the eruption on the feet to have been present for approximately four weeks. The patient described it as having been vesicular at first, then pustular, and scaling and crusting for several days. The urologic department believed the adenopathy to be of fungus origin associated with the eruption of the feet and advised dermatologic consultation in diagnosis and treatment.

Examination.—On July 29, 1927, I first saw the patient. The young man was obviously not acutely ill, but complained of some tenderness in each groin. There were macerated, sodden accumulations with an occasional eroded area between all the toes. Extending back on the dorsum of each foot for several inches was an erythemato-scaling eruption with an occasional crust; the scaling border was well marked, with overhanging edges. Near the internal malleolus of each ankle was an erythematous patch about the size of a dollar, with a well defined, scaling border; the patch on the right ankle was somewhat larger than the one on the left. Visible signs of superficial lymphangiitis were not present on the legs; the glands in the groin were still tender and markedly enlarged, as described. Eruptions of any type had not occurred in the inguinal, crural, perianal or adjacent regions; in fact, there were no cutaneous manifestations proximal to the ankles. The temperature was normal, and the pulse rate was 74; there was no impairment of the peripheral circulation.

Scrapings were taken from the interdigital spaces of the right foot and from the scaling area near the heel of the same foot; 10 per cent potassium hydrate preparations were made, and plantings were made on eight different tubes containing Sabouraud's medium (dextrose). With a small Luer syringe with a hypodermic needle 0.5 cc. of physiologic sodium chloride was injected through surgically cleansed skin into a large discrete inguinal node on the right side, triturated and then aspirated (similar to the technic for gland puncture for *Spirochaeta pallida*). All of the material was planted on three tubes of Sabouraud's dextrose medium. The gland was then excised and macerated in 40 per cent potassium hydrate. Blood culture was also made on the same type of medium. Treatment was instituted as follows: Crude coal tar ointment (Charles J. White's formula) was applied to the feet lesions daily, and cold applications (water bag) were applied to the inguinal areas. The treatments were combined with complete rest in bed.

Laboratory Observations.—After standing for two hours, the extemporaneous potash preparations from the interdigital clefts of the toes and from the scales near the heel showed many long segmented mycelia. The gland preparation was allowed to stand for approximately twenty-four hours in order that it might become as completely cleared as possible; after this, spores and small short broken parts of mycelia were present. Around the sixth day, growth appeared in two of the tubes inoculated with aspirated gland material and in several of the foot cultures (two of the heel and one of the toes), all of which I regarded as *Trichophyton*, probably of the *gypseum* group.

Dr. J. Gardner Hopkins examined one of the cultures from the lymph node of this patient and agreed with my diagnosis, but he was unable to classify it more completely because of a rapidly growing duvet. Dr. Fred D. Weidman was able more thoroughly to determine the morphologic characteristics of the fungus cultures from both the lymph node and the feet, and he considered the recovered organism as *Trichophyton interdigitale*. The latter organism may ultimately be placed in the *gypseum* group, at least as classified microscopically. Dr. Weidman's complete report from the Laboratory of Dermatological Research of the University of Pennsylvania is as follows:

Cultures.—Within two weeks, as grown on dextrose agar (Sabouraud's formula, using an American crude dextrose), the colonies both from the toe and the lymph node had developed to their prime. They were 2.5 cm. in diameter, moderately elevated, loose, fluffy and duveteuse. The margins were sharply indicated and rather abruptly rounded above the surface of the medium. There were no important peripheral mycelial fringes creeping out onto the surrounding surface and no semblance of a moist zone in the periphery, such as is seen in earlier stages of *Trichophyton purpureum*. The center of the colony was elevated into a mound which extended fully 2 or 3 mm. above the general plateau-like surrounding parts of the colony. The color for the most part was a snowy white, but in the more central parts, which surrounded the umbo, there was a faint yellow to a brownish cast. The appearance was good for *Trichophyton interdigitale*. At four weeks the upper parts of the colony became covered by faintly yellowish-brown powder, which was scarcely visible in the lymph node culture, but which was well developed on the toe culture. A few suggestively pink or red discolorations could be discerned on the back of the colony, but not at the margins. The substrate was murky, but not a definitely disclored brown, as is usually seen in *Trichophyton interdigitale*.

Microscopic Examination.—The colonies, as viewed through the walls of the test tube, exhibited tremendous numbers of thyrses sporiferes and engrappes and a few spirals and fuseaux.

In hanging drops, the features were practically those of *Trichophyton interdigitale*. There were not as many thyrses as were seen in the test-tube preparations, and those present exhibited aleuries rather than conidia. In one preparation there were great numbers of engrappes and closely rolled spirals; the segments of some of the latter were particularly swollen and conspicuous, giving a sausage-like appearance to the filaments. There were also numerous fuseaux. A further special feature of the hyphae was a tendency to beading, as Ota[1] figured for *Trichophyton purpureum*. Another was the arrangement of conidia into clusters along the course of the hyphae, such as was recently figured by Benedek[2] for his *Sporotrichum lipsiense* (species novus). A reddish glint pervaded many of the mycelia, but was not reflected in the gross cultures. I do not believe that this color was an optical effect (peculiarity of diffraction, etc.), as it was not exhibited in hanging drop cultures of other species, except *Trichophyton purpureum*. Perhaps it betrays affinities with *Trichophyton purpureum* which are suppressed as it grows in test tubes but released in the hanging drop environment.

Organes nodulares had not developed up to fourteen days.

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1. Ota, M.: Contribution to the Study of Trichophyton Purpurem Bang, Trichophyton Interdigitale Priestley and Trichophyton "B" Hodges, Arch. Dermat. & Syph. **5**:693 (June) 1922.

2. Benedek, T.: Dermat. Wchnschr. **47**:1695 (Nov. 20) 1926.

In short, the organism was the same as that which causes the majority of cases of ringworm of the toe in this section of the United States; and although there were slight differences in morphology, as met in the lymph node and toes, there were no more than those which occur in repeated cultures from one and the same toe lesion. The absence of fuseaux in the original descriptions of Kauffman-Wolff, according to some commentators, may have been an error of omission and should not justify the creation of a new species in the absence of fuseaux, at least until more is known about the constancy with which the "organes" develop in hanging drop even of one and the same strain.

The blood culture was negative for fungi. Complete routine laboratory examinations were carried out. The Wassermann reaction of the blood was negative; the blood count and the differential count were normal; the blood urea was 16.1 and 23.1 on two separate occasions. Eight different single urinary specimens at intervals showed an occasional trace of albumin with a few pus cells usually present.

Clinical Course and Progress.—The temperature and pulse remained within normal limits during hospitalization. Six days later, the glands were much smaller and the eruption on the feet was improving; about a week later, the patient was discharged (Aug. 9, 1927). There has not been any opportunity to examine him since that time.

COMMENT

The relationship between undoubted mycotic foci and certain associated widespread eruptions on the glabrous skin (dermatophytid) is still far from settled, particularly as to the precise route of transference; one moot point is whether the dissemination is always hematogenous or whether it may also be airborne over the surface (manual transference as a probable starting point). Williams [3] recently summarized the known facts and prevailing theories in two excellent papers. Fungi have been recovered from the blood in several instances in severe tinea of the scalp, usually after exposure to the roentgen ray or after the use of fungus vaccines which had initiated the generalized eruption. The presence of organisms in the blood and, presumably their toxins also, would be the most probable cause of such an eruption. Cervical and retro-auricular adenopathy has already been noted in association with kerion of the scalp; in fact, Sutter [4] was able to secure a positive culture of *Trichophyton granulosum* from a softened retro-auricular node, as well as from the original focus (the kerion) and from the associated lichenoid trichophytid.

With the recovery of *Trichophyton interdigitale* from the inguinal lymph node of my patient secondary to a superficial mycotic focus it can

3. Williams, Charles M.: Dermatophytid (Complicating Dermatophytosis of the Glabrous Skin), Arch. Dermat. & Syph. **13**:661 (May) 1926; The Enlarging Conception of Dermatophytosis, ibid. **15**:451 (April) 1927.

4. Sutter, Ernst: Zur Kenntnis der Pathogense der Trichophytide (Skarlatinforme, Lichenoide und Nodöse Exantheme), Arch. f. Dermat. u. Syph. **127**: 735, 1919-1920.

be assumed that fungi can at least occasionally be carried through the lymphatic systems. In patients with lowered resistance or in virulent mycotic infections, the organisms may extend from the lymph system into the blood stream.

SUMMARY

A case is reported of a positive fungus culture of *Trichophyton interdigitale* from an inguinal lymph node associated with and undoubtedly infected secondarily from a superficial fungus eruption of the feet; the same organism was recovered from the primary focus. Such observations of the lymph node have not previously been reported from superficial dermatomycoses.

It is to be emphasized that the primary focus in this case was superficial; it is felt that the particular value in the case reported lies in the fact that fungi may enter the lymphatic glands from such a superficial dermatitis as ringworm of the toes. This dermatitis now appears in the list of focal infections and opens wide possibilities, not only in respect to dermatophytids, but in respect to other widespread dermatoses or even internal states (allergic or otherwise) contingent on local fungus infections.

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HUMAN SWEAT AS A CULTURE MEDIUM FOR BACTERIA

A PRELIMINARY REPORT *

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Hyperhidrosis appears to be an associated factor in many conditions of the skin. Intertrigo, yeast infections, and fungous conditions of the extremities may be mentioned as illustrative of this association. Pyogenic infections, as well, appear at times to be related to hyperhidrosis. In studying the relationship between eczema and disturbance of carbohydrate metabolism, the conclusion was reached that a hyperglycemia was of etiologic significance. The suggestion was made that the hyperglycemia resulted in activation of the pathogenic organisms normally present on the surface of the skin.[1] In view of this observation, an attempt was made to determine whether organisms would grow in human sweat.

Numerous studies have been carried out on the skin flora, the excretion of bacteria and their toxins through the sweat and sweat toxicity. As far as could be ascertained, however, there are no references in the literature to studies on human sweat as a culture medium. An investigation was made, therefore, with three objects in view, namely: (1) to determine whether bacteria grow in sweat; (2) if they do, to compare the growth in sweat with that in other mediums; (3) to note the influence on bacterial growth of sugar content of the sweat.

METHOD OF INVESTIGATION

The subjects in whom sweating was induced were patients selected at random as they entered the outdoor dermatologic clinic of the Montreal General Hospital. All had one skin lesion in common, namely, a localized dermatitis. Pyogenic infections of the skin were not elicited.

The procedure for the collection of sweat was that previously described.[2] No attention was paid to the intake of food or fluid.

The specimens of sweat were slightly turbid, because of the admixture of epithelial debris and other matter. In order to remove the latter, the sweat was cleared by means of kaolin; the chemistry was then studied.

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* From the Departments of Dermatology and Pathology, the Montreal General Hospital, Montreal, Canada.

* Read before the British Association of Dermatology and Syphilology—Canadian Branch, Toronto, March, 1928.

1. Usher, B.: The Relation of Carbohydrate Metabolism to Eczema, to be published.

2. Usher, B., and Rabinowitch, I. M.: Excretion of Sugar in Sweat, Arch. Dermat. & Syph. **16**:706 (Dec.) 1927.

The procedure for the estimation of the sugar content was that previously described.[3] The amounts obtained compared favorably with those formerly reported.

For the determination of the urea nitrogen content, the van Slyke method for the determination of the urea nitrogen in the blood was adopted.

The amount of chlorides in the sweat was determined by the well known silver nitrate principle. The determinations were carried out on the protein-free filtrate.

The presence of amino-acids was tested for, qualitatively, by the biuret reaction. These acids were found in faint traces in all of the specimens examined. Protein was not found. The combined data are recorded in table 1.

After collection, the sweat was sterilized in the autoclave for thirty minutes under 15 pounds of pressure; it was then placed in the refrigerator until required.

The following mediums were used in this investigation: sweat, bouillon with the addition of 0.5 per cent dextrose, 1 per cent dextrose agar slants, sweat agar slants containing 0.12 per cent agar, and Sabouraud's maltose sugar medium.

The following organisms were used in this study: (1) *Staphylococcus pyogenes-aureus,* obtained from a patient with acrodermatitis perstans of the hands; (2) *Staphylococcus pyogenes-albus,* cultured from the eye of a subject with conjunctivitis; (3) *Streptococcus viridans,* cultured from the blood of a patient with Libbman's disease; (4) *Streptococcus nonhemolyticus,* isolated from an abscess in the groin; (5) *Tricophyton interdigitale,* from a patient with ringworm; (6) *Blastomyces,* isolated from a patient with erosio interdigitalis blastomycetica.

TABLE 1.—*Chemistry of Sweat*

	Sweat A	Sweat B	Sweat C	Sweat D
Quantity in cc.	30	200	40	60
Reaction	Ft. acid	Ft. acid	Ft. acid	Ft. acid
Urea nitrogen, per cent	0.036	0.0186	0.027	0.018
Sugar, per cent	0.020	0.006	0.025	0.025
Chlorides, per cent	0.512	0.360	0.424	0.640
Amino-acid	+	+	+	+
Protein	0	0	0	0

Moderately cloudy suspensions of these organisms in saline were prepared. Three cubic centimeter quantities of the various mediums were inoculated with one loopful of the suspension. The higher fungi were allowed to grow at room temperature, the cocci at incubator temperature. The amount of bacterial growth was estimated by the macroscopic appearance of the culture and, where possible, by means of bacterial counts.

RESULTS

All the organisms grew well in sweat and on sweat agar slants.

The growth of the *Staphylococcus pyogenes-aureus* in sweat and in dextrose bouillon was studied in greater detail. Bacterial counts were made at regular intervals from both mediums. The initial growth of this organism was greater in the former medium; it soon became equal in both, but persisted longer in the sweat. The same result was noted in specimens of sweat obtained from three different subjects. The counts are recorded in table 2.

On stock dextrose agar slants, however, growth appeared to be more profuse than on sweat agar slants. Pigment formation was abundant, and was somewhat more pronounced on the latter medium.

The *Staphylococcus pyogenes-albus* grew more profusely and persisted longer in sweat than in dextrose bouillon. This observation is recorded in table 3.

TABLE 2.—*Bacterial Counts Per One Cubic Centimeter of Staphylococcus Pyogenes-Aureus Inoculated Into Sweat and Broth*

Days After Inoculation	Sweat A	Broth	Days After Inoculation	Sweat B	Broth
4	20,000	4,000	1	16,000	13,000
11	16,800	5,300	3	20,540	13,700
16	4,100	4,800	8	5,600	5,500
22	1,775	1,410	14	1,330	1,465
28	1,700	.....	20	350	.....
33	580	.....	25	32	.....
37	...	.....	29	..	.....

TABLE 3.—*Bacterial Counts Per One Cubic Centimeter of Staphylococcus Pyogenes-Albus Inoculated Into Sweat and Broth*

Days After Inoculation	Sweat C	Broth
1	110,000	66,000

TABLE 4.—*Bacterial Counts Per One Cubic Centimeter of Streptococcus Viridans Inoculated Into Sweat and Broth*

Days After Inoculation	Sweat B	Broth
5	1,720	833
8	1,405	750
11	2,600	2,830
20	878	720
30	...	...

TABLE 5.—*Bacterial Counts Per One Cubic Centimeter of Streptococcus Nonhemolyticus Inoculated Into Sweat and Broth*

Days After Inoculation	Sweat B	Broth
1	866	3,770
3	440	420
6	1,100	1,420
15	460	600
25	...	50

Similar results were obtained with the *Streptococcus viridans*. Table 4 details the results.

The counts of the *Streptococcus nonhemolyticus* are recorded in table 5. This organism appeared to grow somewhat better in the dextrose bouillon.

The higher fungi grew more profusely in the sugar mediums than in sweat. Bacterial counts of the *Tricophyton interdigitale* could not be

made. This fungus commenced to grow sooner on sweat agar slants than on Sabouraud's medium. Pigment formation, as well, was much more pronounced on that medium; it was almost negligible on sweat agar.

The growth of the yeast was studied macroscopically and by means of counts. The latter could only be approximate, because clumping was so marked. Growth in dextrose bouillon was greater than in sweat. Growth was still present in both mediums eight weeks after inoculation. Similar results were obtained on samples of sweat obtained from three different subjects. The counts are recorded in table 6.

Table 6—Bacterial Counts Per One Cubic Centimeter of Yeast Inoculated Into Sweat and Broth

Days After Inoculation	Sweat B	Broth
5	16,000	24,000
10	5,600	5,000
29	750	1,250

Table 7.—Bacterial Counts Per One Cubic Centimeter of Staphylococcus Pyogenes-Aureus Inoculated Into Sweat and Broth

Days After Inoculation	Sweat A	Sweat B	Sweat C
5	25,000	15,000	40,000

TABLE 8.—*Bacterial Counts Per One Cubic Centimeter of Staphylococcus Pyogenes-Aureus Inoculated Into Sweat and Broth*

Days After Inoculation	Broth	Sweat D	Sweat D + 0.012% Dextrose	Sweat D + 0.025% Dextrose
1	17,500	26,000	93,000	480,000
6	.....	18,200	.....	42,000
13	.....	25,000	35,000	37,500

The yeast showed more profuse growth on both Sabouraud's medium and dextrose agar slants than on sweat agar slants. Pigment formation, too, was much more pronounced on the former mediums.

Specimens of sweat from three different persons were inoculated with the *Staphylococcus pyogenes-aureus*. Growth was not equally active in all the specimens. It was least active in specimen B, which contained only 6 mg. of sugar per hundred cubic centimeters, and most active in specimen C, with a sugar content of 25 mg. per hundred cubic centimeters. The counts, made on the fourth day after inoculation, are recorded in table 7.

This variation in growth appeared to depend on the sugar content of the sweat. To determine whether this observation was accidental or real, the *Staphylococcus pyogenes-aureus* was planted in specimens of

sweat to which varying amounts of chemically pure dextrose had been added. From a study of table 8, it may be noted that bacterial growth appeared to vary directly with the sugar content of that medium.

CONCLUSIONS

Human sweat has been shown to be an excellent culture medium for certain bacteria, including various higher fungi.

Comparative studies reveal that it compares favorably, as such, with various laboratory mediums.

The activity of bacterial growth in sweat appears to vary directly with the sugar content.

I wish to take this opportunity of thanking Dr. F. E. Weidman, University of Pennsylvania Medical School, through whose courtesy the *Tricophytom interdigitale* and the yeast were obtained.

SCLERODERMA-LIKE EPITHELIOMA

DOUGLASS W. MONTGOMERY, M.D.
AND
GEORGE D. CULVER, M.D.
SAN FRANCISCO

A recognition of the different clinical appearances of epitheliomas is of great importance in determining the treatment to be employed. This statement applies decidedly to the scleroderma-like epitheliomas.

CLINICAL CHARACTERISTICS

This neoplasm grows slowly, and does not cause pain or other disturbance until late in its course and after it has attained considerable dimensions. Even then it is painless, and the patient's attention is finally drawn to it by a shallow easily bleeding ulcer that appears in the center of its field and refuses to heal, or if it temporarily heals, it quickly opens again. Sometimes the little ulcer is the only obvious feature, and the characteristic yellow, smooth field in which it is situated is perceived only when attention is drawn to it.

Appearance.—The epithelioma is usually a small, circular, flattened plaque not more than a centimeter in diameter. It is either white or more frequently an ivory yellow, smooth and devoid of any of the cross-markings of the skin, and looks like a patch of morphea or scleroderma. As is usual with epitheliomas, the border is abrupt and slightly raised. The surface is streaked with bright red convergent capillaries.

TREATMENT

Radiant Energy.—The diagnosis of epithelioma having been made, one naturally recurs to radiant energy, either roentgen-ray or radium, for treatment. This mode of treatment, in this epithelioma, encounters serious disadvantages. The more embryonic the type of the epithelial cells in a given epithelioma, the more succulent the cells are, and the more exposed the cell nucleus is when undergoing growth by division, the more efficient is the action of the roentgen rays or radium. On the contrary, however, the nearer the tumor cells approach the normal type of cells in their vicinity, the less are they affected by the roentgen rays or the gamma rays of radium. The epithelial cells of this scleroderma-like type of epithelioma are nearly normal, and in order to affect them detrimentally and secure a cure, irradiation has to be carried out to its cauterant effect, and gamma or roentgen rays are poor cauterants. There are many better ones, both chemical and physical. They make a severe burn, one that heals slowly and one that is inevitably followed

by disagreeable after-effects. The best treatment is first to curet out thoroughly and then apply radium heavily screened. We employ a plaque the size of a ten cent piece containing 25 mg. of radium, screened with 2 mm. of lead and two of rubber, held in place for five hours. This will affect the soft deeper cells which are not yet cornified, and has the further advantage of securing a flat, smooth, almost unobservable scar.

REPORT OF CASES

Case 1.—A physician, aged 60, consulted us on Dec. 7, 1927, for a scleroderma-like epithelioma with a small ulcer in the center of its field, situated on the right side of the nose, level with the eye. The whole lesion was a little over a centimeter in diameter, which is a considerable area in this situation. At a distance, the scleroderma-like infiltration could not be seen, but under a lens, it stood out distinctly. The patient said that he had first noticed the condition two years before, and that one year previously he had been treated with radium for four hours, but the condition had recently reappeared. When he consulted us, there was a small narrow ulcer covered by a blood-stained crust, and it was only by examining it more closely that the extent of the disease area could be appreciated. It was a smooth, flattened, circular, ivory yellow area with an abrupt rounded border, and there were a number of bright red capillaries coursing over its surface and converging on the small ulcer. It is the discovery and the just appreciation of the extent of this diseased area that constitutes the main point in the diagnosis. We have seen a surgeon cut through such an area and a prompt, and to him, satisfactory healing followed. As the neoplasm is an exceedingly slow one, the inevitable recurrence of the ulceration after such an operation may be delayed for a year, that is to say, for as long as the recurrence following the radium treatment in the case here related.

Case 2.—Years ago one of us, in company with Dr. George Chismore and Banjamin F. Swan, saw an example of this neoplasm that occurred on the inner leaf of the prepuce and in the sulcus in an elderly man. The lesion was ivory yellow, and had a smooth, shiny, cupped surface and rounded borders. Transversely to the penis its surface was convex, but in the antero-posterior direction it was concave. The lesion, therefore, represented a plate bent in two directions. It was extremely large, measuring about one inch (2.5 cm.) by three-quarters of an inch (2 cm.). Although it was so large, ulceration could not be observed either clinically or microscopically. The microscopic section showed the lesion to be entirely covered with a thin layer of epithelium, and beneath this there was the epithelial infiltration of epithelioma. Its prominent rounded borders, its cupped surface and its induration gave it a remarkable resemblance to chancre; also, on retracting the prepuce, the lesion snapped over just as a chancre would. In the Baretta models of the St. Louis Hospital in Paris, there is a similar case in which the lesion occupies the same situation.

Case 3.—A woman, aged 27, consulted us on Aug. 8, 1916, for a nonulcerated centrally contracted morphea-like epithelioma of the lower eyelid. Curetting laid bare a large, shallow semilunar surface with a good margin of sound tissue between it and the edge of the lid. We cauterized the raw surface with acid mercuric nitrate and then irradiated it with the roentgen rays. It was before we had radium, or this would have been employed. The result was good; a smooth, flexible scar remained and there was no eversion of the lid.

CONCLUSION

As an epithelioma consists anatomically of an epithelial infiltration, an important and never to be omitted part of the technic of diagnosis is to examine the edge of the lesion, which is usually rolled and abrupt with dilated capillaries coursing over its surface. The capillaries, being above the infiltration, show clearly that the infiltration lies in the connective tissue, as capillaries can run only in connective tissue; therefore, the infiltration is clearly in the connective tissue, not on it, which is the essential anatomic requirement of epithelioma. At times the infiltrating epithelial cells degenerate so quickly that the rolled advancing border cannot be made out. In some cases the border is well marked, and the ulcer lies within it. In other cases there is an advancing border and within it a narrow, ulcerating ditch encircling a cicatrizing center, in which all the infiltrating epithelial cells have died out, leaving only connective tissue. In still other cases the infiltrating epithelial cells are more permanent and spread out into a broad thin plate, but they have the rolled advancing border. These form the scleroderma-like epitheliomas, the subject of this paper. When the infiltration extends far out, the capillaries fail to carry the required nourishment to the center, and ulceration takes place, as in the first of our cases cited.

In the case of the gigantic subpreputial epithelioma, the protection afforded by the prepuce delayed the central ulceration which undoubtedly would have taken place on an exposed surface. In the third case reported, the central area underwent cicatricial contraction instead of ulcerating.

Bearing these facts in mind, and especially the varying viability of the epithelial cells, one can reach some conclusion as to the extent to which one may rely on radiant energy or on an operative procedure or may with advantage employ both.

XERODERMA PIGMENTOSUM

UNUSUAL IMPROVEMENT IN ONE MEMBER OF AN AFFECTED FAMILY

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AND
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PHILADELPHIA

Xeroderma pigmentosum is a disease which usually does not show a tendency to regression, although it is frequently noted to remain stationary for a number of years. A cured case is practically unknown. The tendency is decided progression toward a fatal ending, although that termination may be some years distant.

It is with the thought that the prognosis may sometimes be too severely expressed that we report the unusual remission in this case.

REPORT OF A CASE

History.—The patient, C. H. D., a white boy, aged 8, an American, had a rather significant history. His parents were first cousins, and both were decided blonds. There were six children in the family of which number the patient was the youngest. The mother died of influenza and pneumonia on the day the patient was born. Her skin was extremely fair and without blemish. The father is living and healthy. His complexion is rather ruddy.

The first child, a girl, died of a condition diagnosed as jaundice, when 9 days old.

The second child, L. M. D., showed the first incidence of xeroderma pigmentosum. At the age of 2 years, she developed a rather large wart on the side of the nose. This was the first evidence of skin trouble, save that her face, neck and arms were unusually ruddy and freckled. Other growths appeared on the face. Finally, a large cauliflower growth entirely covered the right cheek and closed the right eye. From this tumor, a hemorrhage occurred which caused the child's death at the age of 7 years. The covered portions of the body did not exhibit any changes in the skin.

The third child, a boy, aged 17, is living. He has a fair skin which freckles readily. His body is covered with a marked growth of fine blond hair.

A girl that died in infancy was the fourth child. She had an enlarged liver, first noted after an operation.

The fifth child, K. D. D., a boy, developed freckles when but a few weeks old. These spots were only on the exposed parts of the body. Dr. H. H. Hazen, of Washington, attended the child from the beginning of the disease. In a recent letter, he gave the diagnosis as xeroderma pigmentosum. A mask was found to be difficult to retain in place, and the use of a thick paste was impracticable for so young a child. After spongy growths had appeared, roentgen-ray treatments were employed, and destruction was tried by other means. Before his death at the age of 4 years, a succession of growths had extended almost half way around the left side of the neck.

The present patient and sixth child, C. H. D., was brought to the Jefferson Hospital (skin dispensary) by Dr. William H. Kraemer, of Wilmington, Del., on

March 7, 1927. His skin condition had begun later than was the case in the other members of the family. He freckled readily. Two or three years before he came under observation, small warty growths were first noticed on the right cheek. They spread over the nose, the left cheek and around the mouth; in a few months these growths had become extremely noticeable, especially after he had been outdoors. His eyes were sensitive to strong light. The skin on the back of the hands was rather rough and at times seemed extremely dry. There were small, pinkish spots on the face. The patient often complained of severe pain in the legs, which was a symptom common to the two other affected children. With the exception of the last child, all these children had been bottle-fed babies and had been difficult to feed. The family felt that this child had a better start, and that as a consequence the disease had begun later in life than in the other two. He was healthy. He was in his proper grade at school. Only moderate care had been taken to prevent exposure to sunlight.

Examination.—Examination of the patient showed a markedly undersized child of about the weight and proportions of a boy of 5 years. He was mentally alert, though somewhat depressed, as he realized the significance of his trouble. His complexion was extremely fair, and he had flaxen hair. Slight photophobia was noted in a well lighted room. The skin of the face was markedly freckled and dry and had a tendency to scale.

This appearance continued from the hair to the collar line, being less noticeable under the chin. On the cheeks were numerous flat warts, especially evident about the nasolabial folds and sides of the nose. Occasional mottled areas of pinkish depigmentation were noted on the face. The backs of the hands and wrists were dry, freckled and rough. There were no definite telangiectases or epitheliomas, but this seemed to be a clear case of xeroderma pigmentosum even without the evidence of the history.

Treatment and Course.—We explained to the guardian the methods of protection that we wished to have enforced against the sun, wind and cold. A thick protective salve was prescribed, and advice was given to keep the child away from the seashore or other unusually sunny places. He was told to wear a broad brimmed hat, avoid outdoor sports, such as baseball, and use the ointment prescribed much of the time.

The patient returned to Delaware, and we did not hear from the family again until November, 1927. The boy was then again brought to see us, and a remarkable change was noted. The dryness, roughness, freckles and warty growths had all disappeared, and his skin was normal. The patient, doubtless impelled by fear of consequences, had given his greatest cooperation to the earnest efforts of the family. He had worn his protection, had always played in the shade when outdoors and had stayed closely at home. During the nine months' period since we had seen him, a startling improvement had been effected in spite of the fact that this period included the sunniest part of the year.

COMMENT

While this patient's condition is undoubtedly milder than was that of either of the other members of the family, it seems worth while to record the improvement under a certain regimen, temporary though that improvement may be.

Medical Arts Building, 2035 Spruce St.

RADIUM THERAPY OF TUMORS OF THE SKIN AT THE CURIE INSTITUTE OF THE UNIVERSITY OF PARIS*

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BIRMINGHAM, ALA.

At the time of the initial visit of a patient with cancer of the skin, an immediate biopsy is performed. This is an absolute prerequisite for treatment, as the authorities believe that even when the diagnosis of cancer is evident, histologic study will reveal information concerning the variety and the radium sensitivity of the tumor in question which will be invaluable for postradiation statistical analyses.

If the tumor has been treated by radium or roentgenotherapy elsewhere, the patient is not eligible for admission to the clinic. This is not a hard hearted policy, because the Curie Foundation is not for immediate charity but for the purpose of bettering the existing methods of treatment of cancer and to establish a rational, scientific basis for radium therapy. This necessitates the primary treatment of the cancer; otherwise the variable dosage of roentgen ray used in other institutions, the lack of the original histologic data and the factor of acquired radioresistance unite to confuse the radium therapist. In treating persons with malignant conditions by radium, if at first one does not succeed, one cannot try, try again, with any certainty of success.

If the dosage of roentgen ray is great but insufficient or incorrectly timed or incorrectly spaced, then within from six weeks to two months the tumor may develop a radioresistance which persists indefinitely. Treatment with roentgen ray is never successful after radium has failed: on the contrary, patients with recurrences after roentgen-ray treatment are occasionally susceptible to treatment by radium. When association of the two modes of radiation is purposely planned, it is advisable to have the roentgenotherapy precede the treatment by radium.

TREATMENT

The focal distance of the radium from the skin depends on the nature and the type of the lesion to be treated. This distance is obtained by the intervention of a wax which is transparent to the gamma rays of radium. The formula for this wax is 100 Gm. of pure beeswax, 100 Gm. of paraffin fusible at 62 C. and 20 Gm. of finely sifted sawdust. This mixture is melted into sheets 1 cm. thick. It softens readily in hot water

*From the Department of Pathology, School of Medicine, University of Alabama, Tuscaloosa and the Seale Harris Clinic, Birmingham.

at 48 C., and is molded over the tumor until it hardens into a permanent moulage. The mixture can be sterilized at 120 C. and used again. It is said that this wax has approximately the same absorption coefficient as the skin. It is also maintained that, unlike dental modeling compound, it does not give off any secondary beta rays during gamma permeation. If the cancer of the skin is small and flat, the focal distance may be only 0.6 cm., but if it is an elevated or a large lesion, the distance is correspondingly greater, as from 1 to 1.5 cm.

The epidermoid cancer of the skin is composed of cells in the process of cellular differentiation or evolution, so that any line of cells goes through alternating phases of reproductive activity and quiescence. During the period of repose or rest, the cell is somewhat radioresistant; during the moments of cell division or mitosis, the cell is most sensitive to the lethal action of radium. Consequently, the time of application of the radium is extended over a minimum of five days in order to destroy the "mother cells" which divide at successive intervals, and therefore at some time pass into this phase of maximal sensibility. Treatment of eight hours daily for five days is the customary procedure, but this may be modified according to the amount of radium available. The time is never less than five days, but may be as many as eight days, and the radium may be applied for twelve hours daily in order to obtain the required dosage, although eight hours daily is preferable. The amount of filtration is always 1 mm. of platinum.

In America the dosage is expressed in terms of "milligram hours" or "millicurie hours," which is a constant value, being the dose of emission of radium. It is easily computed by multiplying the intensity of the radiation (i.e., quantity; milligrams of radium or millicuries of radium emanation utilized) by the duration in hours of the application. The notation dosage used throughout France makes the dose proportional to the quantity of radium destroyed during the course of its application; this notation (Debierne and Regaud, 1914; Regaud and Ferroux, 1919) is preferable because it is commodious and equally applicable to tubes of radium or of radon. Let it be assumed that the total therapeutic value of 1 millicurie of radium emanation is 133 millicurie hours. Therefore 1 millicurie destroyed is the equivalent of 133 millicurie hours or of 133 milligram hours, or 1 mg. of radium acting for 133 hours may be expressed in terms of dosage as 1 millicurie destroyed. One millicurie destroyed is equal to 1,000 microcuries destroyed. The radium is used in platinum tubes each containing 6.66 mg. of element, which gives radiations equaling 50 microcuries destroyed hourly.

The dosage of radium is variable, depending on the size of the lesion. For a small epidermoid cancer, such as one 2 sq. cm. in area, the dose may be as high as 4½ millicuries destroyed per square centimeter of

tumor; but for larger cancers, such as one measuring 25 sq. cm. in area, the dose is often only 2 millicuries destroyed per square centimeter of tumor.

Two illustrative cases are given for the purpose of demonstrating the principles of dosage.

REPORT OF CASES

CASE 1.—A man had an ulcerating epidermoid carcinoma of the left temple. The area of the cancer was 56 sq. cm. The area to be irradiated was 60 sq. cm. The focal distance was 2 cm. by wax moulage. The amount of filtration was 1 mm. of platinum. The basic dosage was 2 millicuries destroyed per square centimeter (266 millicurie hours). The total dose was two times 60 sq. cm. equaling 120 millicuries destroyed or 15,960 millicurie hours. As treatment was continued for eight days, the amount of millicuries destroyed (120) divided by the time of treatment (eight days) equals the amount (15 millicuries) destroyed daily, 1,995 millicurie hours. Eighteen tubes of radium, each containing 6.66 mg. were used. The use of 6.66 mg. of radium for one hour is equivalent to 50 microcuries destroyed. The number of radium tubes used (18) multiplied by the number of microcuries destroyed hourly (50) equals 900 microcuries or 0.9 millicuries destroyed hourly. Since the patient is to receive 15 millicuries destroyed daily, this amount (15) divided by the amount destroyed hourly (0.9) equals sixteen hours and forty minutes, the length of time daily this amount of radium should be applied.

CASE 2.—A large, vegetating epidermoid cancer was noted on the left temple of an old lady. The area of the skin to be irradiated was 65 sq. cm. The focal distance of radium from the skin was 2 cm. (obtained by wax). The amount of filtration was 1 mm. of platinum. Thirty-two tubes of radium were employed, each containing 6.66 mg. of radium. Since 6.66 mg. of radium equals 50 microcuries destroyed hourly, the intensity of the radium (32) multiplied by the number of microcuries destroyed hourly (50) equals 1,600 microcuries or 1.6 millicuries destroyed hourly. The dose is 2 millicuries destroyed per square centimeter. The number of millicuries (2) destroyed multiplied by 65 sq. cm., the area to be irradiated, equals 130 millicuries destroyed, or the total dose. The amount of millicuries (130) destroyed divided by the number of millicuries destroyed hourly (1.6) equals the number of hours of treatment necessary, 81¼. Ten days are employed for the treatment. Therefore the amount of hours (81¼) necessary for treatment divided by the number of days (10) required to complete the treatment gives a total of eight hours and seven minutes, the amount required for each daily treatment.

COMMENT

In nonepidermoid cancer of the skin, more familiarly known in America as the basal cell cancer, the time specification of five days is not so essential, and the dose may be given quickly. This dose of radium is about the same as the total for epidermoid carcinoma, although the latter is more easily cured locally by irradiation.

An interesting observation made at the Curie Institute is that the majority of epitheliomas arising in lupus lesions do so after futile attempts have been made to cure the lupus by poorly administered roentgen-ray treatments.

Melanosarcoma and melanocarcinoma are considered unsuitable tumors for radium therapy because of their recognized natural radioresistance. Electrocoagulation is the preferred method of treatment.

Hemangiomas of the skin are treated by surface irradiation if they are superficial. Near the orbit, it is better to employ electrolysis than radium, because of possible injury to the eye by the latter. In other locations, the thick hemangiomas of the skin are treated by radium puncture needle (interstitial radiation). The filtration is only 0.2 mm. of platinum because the effect of the beta rays is desired. The dosage, however, is light, only about 0.5 millicurie destroyed (67 millicurie hours) for each square centimeter of the surface area of the hemangioma.

I wish to express my gratitude to Professor Claude Regaud, Director of the Radium Institute of the University of Paris, and his able colleagues, Dr. Lacassagne, Vice-Director, Dr. Monod, radium therapist, and Mlle. Thurnyssen, for the information contained herein and for the kindness shown to me during my studies in their institute.

AN EFFICIENT TREATMENT FOR VARICOSE ULCERS

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NEW YORK

In 1924, W. Lowenfeld [1] made a thorough study of the bacteriologic and histologic characteristics of ulcers of the leg. The results of cultures in fifty-one cases of ulcer of the leg revealed the following organisms: *Staphylococcus*, 44 cases (*Staphylococcus aureus*, 20; *Staphylococcus albus*, 24); *Streptococcus*, 22 cases; *Diplococcus lanceolatus*, 3; pseudodiphtheria bacillus, 5; *Proteus vulgaris*, 17; *Pyocyaneus*, 8; *Bacterium coli*, 10; *Micrococcus tetragenous*, 1; *Bacterium mesentericus*, 1; sterile, 1. None of these bacteria could be viewed as specific. *Staphylococcus* and *Streptococcus* were found alone in the largest percentage of cases (*Staphylococcus* alone eleven times, and with *Streptococcus* eighteen times; *Streptococcus* alone fifteen times and with other bacteria thirteen times). With the reduction of the number of bacteria through treatment, there was progressive healing. Histologic examinations have shown that a number of bacteria become progressively less according to the depth of the tissue examined. The greatest number are present on the surface of the tissues. Apparently, as in the normal healing of a wound, the natural defense of the new formed granulations prevents bacteria from getting deeper into the tissues. In the callous forms, the resistance may be due to the fibrous tissue.

In view of the rich bacterial flora of the ulcer, it occurred to me to attempt a general sterilization of the wound. After trying the known methods unsuccessfully in all of my private cases, twelve in number (in none of which there were positive Wassermann reactions), I employed an ointment of 1 per cent neoarsphenamine with the most gratifying results. A layer of this ointment was applied only once, at night over the surface of the wound. The treatment proved painful, so an anesthetic was added as follows: neoarsphenamine, 0.3 Gm.; ethylaminobenzoate, 2 Gm.; white petrolatum, 30 Gm. After one application, a 10 per cent bismuth subgallate ointment was applied for the next few days.

The depth of the ulcer diminished one half after the first treatment.

The edges became clean, and a crust formed under the tissue, which soon raised to its normal level.

Two and three years have elapsed since the treatment of these patients, but the ulcer has not recurred in any case. The site of the ulcer is covered with a pigmented scar area.

It is my hope that this method will be tried, and that it will prove a profitable addition to the therapy of varicose ulcers.

485 Park Avenue.

1. Lowenfeld, W.: Bacteriology of Leg Ulcer, Wien. klin. Wchnschr. **37**: 502 (May 15) 1924.

Clinical Notes

BENIGN CYSTIC EPITHELIOMA: REPORT OF A CASE

F. J. Eichenlaub, Washington, D. C.

A colored boy, aged 12, had an eruption on the face of six years' duration. The onset was gradual, a few isolated papules appearing at first; these had gradually increased in number, and in several places had coalesced. At the time of examination, he presented an eruption on the eyelids, nose and both sides of the face. In several places, the confluence of papules had produced circinate papular and solid nodular lesions. The lesions were not deep; they were hard to the touch, did not show any evidence of inflammation and were slightly darker than the normal skin.

The boy also had interstitial keratitis and other evidence of congenital syphilis, with a 4 plus Wassermann reaction.

Biopsy showed the typical picture of benign cystic epithelioma, i. e., groups of basal staining epithelial cells in the corium, with cornification and cystic formation in the center of the lesion.

The case is recorded because of the race and youth of the patient and the presence of large lesions due to confluence of smaller papules.

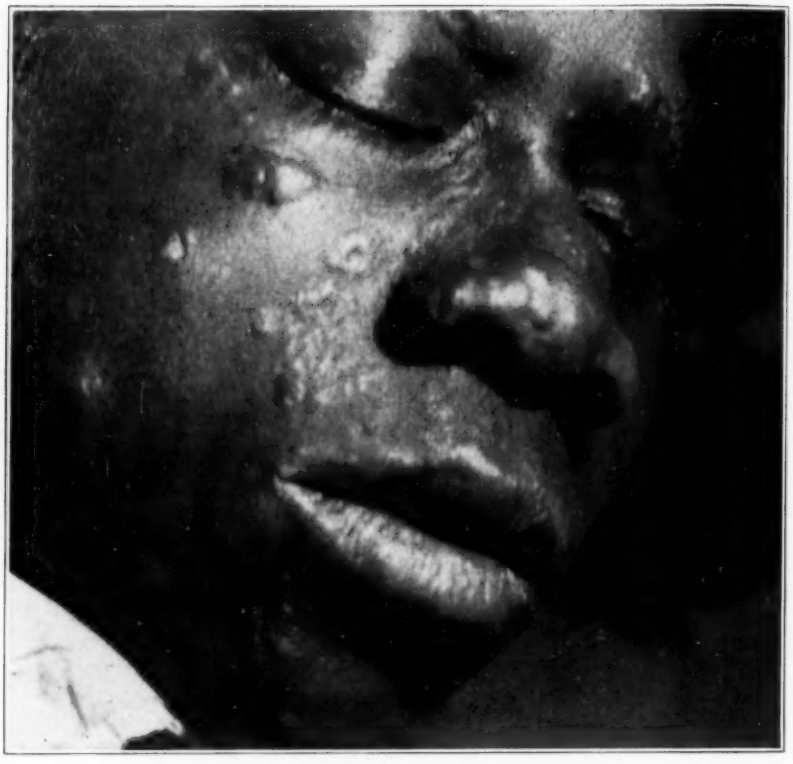


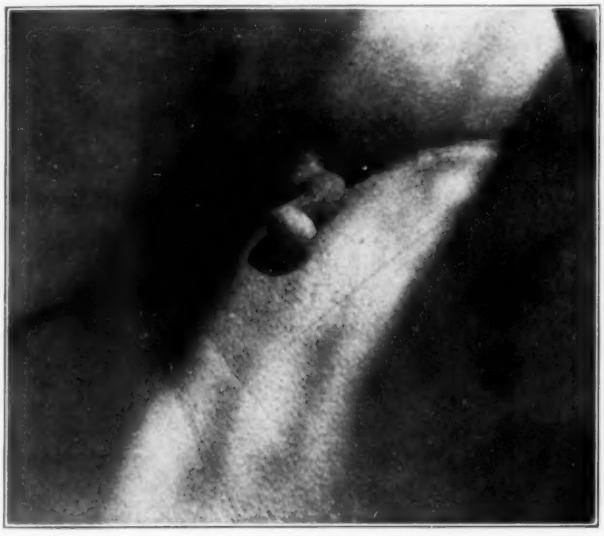
Fig. 1.—Lesions on face.

Fig. 2.—Low power photomicrograph from lesion excised from cheek.

AN UNUSUAL APPENDAGE OF THE ANAL REGION IN A MEXICAN WOMAN

G. P. LINGENFELTER, M.D., DENVER

S. V., a Mexican woman of the peon type, aged 23, was admitted to the Denver General Hospital on Aug. 13, 1927, to be confined. On examination, the unusual growth which is illustrated was discovered; the patient denied all previous knowledge of its existence. The growth is 3⅛ inches (7.63 cm.) in length and ¾ inch (1.9 cm.) in circumference at the base, gradually tapering



toward the distal extremity. When curled up, its habitual attitude, it closely resembled a pig's tail. It arose from, and was apparently intimately connected with, the external anal sphincter, being located at the anterior and the left lateral aspect of the anal opening. Distinct movement of the growth was noted on dilatation and contraction of the sphincter, while during labor pains the growth would straighten out as though composed largely of erectile tissue. It was not a prolongation of the coccyx, and no bony structure was found. The growth was covered with normal appearing skin of the same color as the surrounding parts and had a sparse growth of hair. Biopsy was refused.

CORRECTION

In the transactions of the Brooklyn Dermatological Society (ARCH. DERM. & SYPH. **18**:146 [July] 1928), the word "chlorate" in the fourth line of Dr. Abramowitz's discusson, on page 147, should read "chloride."

Editorials

TRADITION IN DERMATOLOGY

The address of Dr. Wile, Chairman of the Section on Dermatology and Syphilology of the American Medical Association (The Perpetuation of Error in Dermatology, J. A. M. A. **91:** 219 [July 28] 1928) contains a good many timely suggestions about the mischievousness of carelessly relying on tradition. He refers to the value of accumulated knowledge of masters of long experience and of the weight that should be given to their observations, but he also calls attention to the fact that there is danger in uncritical acceptance of all that they have done. Times change, and we know more about some factors in dermatology now than we once did. What Erasmus Wilson or Hebra set up as a definite disease, based on symptomatology alone, may be merely a symptom complex, not a disease at all, but a manifestation of several diseases.

Dr. Wile called attention to an immense amount of needless error, resulting from faulty quotations from the literature. Another pernicious habit is that of copying bibliographies wholesale—"bibliographies"—as one reviewer once said—"as complete as money can buy." It is a cheap display of pseudolearning, which is useless and often confusing. In spite of all the care that one can use in sifting the work of former masters, in transcribing the literature and in one's bibliographies, a certain amount of error is inevitable. The errors, however, which are constantly perpetrated through "trustful adherence to constituted authority" and through medical misquotation, do not have any place in the literature, and they can be in large part avoided by cultivation, by critical consideration and by careful reporting of the work of others. Work that is worth referring to is deserving of at least that much attention.

W. A. P.

News and Comment

News from France.—Dr. G. Petges has succeeded Dr. William Dubreuilh as Professor of Dermatology at Bordeaux.

Dr. L. Joulia has been appointed Professeur agrégé of Dermatology at Bordeaux.

Dr. Jean Gaté has been appointed Professeur agrégé of Dermatology at Lyons.

Abstracts from Current Literature

TUMORS OF THE BRAIN AND SYPHILIS. F. P. MOERSCH, Am. J. M. Sc. **175**:12, 1928.

In an analysis of 1,000 cases of tumor of the brain, the Wassermann reaction was found to be positive in eighteen, although the possibility of syphilis was considered seriously in only four of the eighteen. In only one case was the spinal fluid positive; this case did not show any evidence of syphilis clinically or at operation. Unusual observations of the spinal fluid might suggest a therapeutic test to aid in the diagnosis, and choked disk may be found frequently enough in cases of syphilis to preclude its acceptance as positive evidence in cases in which tumor of the brain is suspected.

ACTINOMYCOSIS: A REPORT OF FIVE CASES WITH FOUR AUTOPSIES, TWO SHOWING INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM. P. O. SNOKE, Am. J. M. Sc. **175**:69, 1928.

Each initial lesion in these cases was located in a different area, namely: the jaw, chest wall and lung, vertebrae and lung, abdomen and tongue. Two cases showed a definite involvement of the central nervous system.

Radium and the x-ray were considered of great value in the treatment of lesions near the skin. The iodides should be administered in as large quantities as can be tolerated, and abscesses should be drained as indicated.

HEREDITY IN HEMOPHILIA. M. T. MACKLIN, Am. J. M. Sc. **175**:218, 1928.

The laws of heredity governing the transmission of hemophilia are summarized briefly by Macklin. A man afflicted with hemophilia will not have children showing this disease, provided he marries a normal woman who is not a carrier. The sons of such a man will be normal and cannot transmit the defect, but the daughters, outwardly normal, will be carriers. Half of the daughters of a female carrier are apt to be carriers, and if there were a woman with hemophilia, all her sons would have the disease.

Only unaffected men and their descendants can marry with impunity, and women carriers should not reproduce.

THE THERAPEUTIC MECHANISM OF MALARIA. TREATMENT OF GENERAL PARALYSIS. OBSERVATIONS ON A CASE. W. H. GOECKERMAN, Am. J. M. Sc. **175**:261, 1928.

In this case report, the occurrence of a tertiary syphilid was noted five months after malaria treatment for general paralysis, during which period there was a marked improvement in the patient's mental and physical state.

It is suggested that the malaria treatment reestablished a partial immunity, the skin playing a definite part. The gradual improvement in the spinal fluid would further support the idea that the results of inoculation depend on a reaction of the tissues rather than on a direct spirocheticidal effect.

EFFECT OF ONE HUNDRED INJECTIONS OF TRYPARSAMIDE UPON THE SPINAL FLUID IN GENERAL PARALYSIS. H. A. BUNKER, JR., Am. J. M. Sc. **175**:265, 1928.

Tryparsamide is considered the best arsenical compound to use in cases of neurosyphilis, but it is stated that the best results are not to be obtained with less than 60 injections; preferably 75 to 100 or more should be given. Complete negativity of the spinal fluid may possibly be obtained with the larger number of treatments.

THE BORDER ZONE BETWEEN THE HYPERPLASTIC AND NEOPLASTIC PROCESSES OF CUTANEOUS EPITHELIUM. F. D. WEIDMAN, Am. J. M. Sc. **175**:479, 1928.

Attention is directed to apparent discrepancies in the pathologic and clinical appearances of such conditions as pigmented nevi and benign anomalies of sweat glands and hair follicles, these lesions having the microscopic picture of carcinoma yet being clinically benign growths.

Exceptionally rapid cutaneous regeneration may also simulate carcinoma; mitotic changes, together with deep permeation below the level of the sweat glands, may be the essential criteria in some cases.

Neoplasia and hyperplasia of the secretory portion of the sweat glands are rare, as well as neoplastic changes in the sebaceous glands, though hyperplasia is said to occur in rosacea and the seborrheic states.

JAMIESON, Detroit.

PORTAL CIRRHOSIS ASSOCIATED WITH CHRONIC INORGANIC ARSENICAL POISONING: REPORT OF TWO CASES. P. A. O'LEARY, A. M. SNELL and E. G. BANNICK, J. A. M. A. **90**:1856 (June 9) 1928.

The authors report two cases of portal cirrhosis with ascites, following the long continued ingestion of inorganic arsenic. Each patient presented definite arsenical lesions of the skin. The symptoms of cirrhosis disappeared in each case after the arsenic was stopped. Arsenical cirrhosis is a definite entity, in the opinion of the authors; the history, course, previously reported similar cases (which are reviewed) and response to treatment are cited to support their point of view.

DERMATOPHYTOSIS OF EXTREMITIES WITH PERIPHERAL OCCLUSIVE ENDARTERITIS: PRELIMINARY REPORT OF CLINICAL AND THERAPEUTIC OBSERVATIONS. C. WHITE, J. A. M. A. **90**:1865 (June 9) 1928.

In a series of eighteen patients who had resistant dermatophytosis of the extremities, examination of the peripheral blood vessels revealed an obliterating occlusive endarteritis. This circulatory impairment seemed to be a factor in favoring the development of the mycotic dermatitis, even to the production of ulceration.

Three of the cases are recorded in detail. In these cases, sodium citrate intravenously appeared to have a favorable influence, after various local measures had failed.

ACNE FROM IODIZED SALT. B. SHELMIRE, J. A. M. A. **90**:1869 (June 9) 1928.

Shelmire reports several cases of acne vulgaris, apparently due to the use of iodized table salt. His patients were all women, most of them past the "acne age." The relation of the iodine intake to exacerbations of the acne was unmistakable.

CHROME ULCERS: REPORT OF TWELVE CASES. J. BLAIR, J. A. M. A. **90**:1927 (June 16) 1928.

The patients in this series were engaged in chrome plating. Eight had ulcerations on the hands and fingers; four had ulcerations or perforation of the nasal septum.

VARICES OF THE LOWER LIMBS: TREATMENT BY OBLITERATING INJECTIONS BASED ON EXPERIENCE WITH MORE THAN FOUR THOUSAND INJECTIONS. J. FORESTIER, J. A. M. A. **90**:1932 (June 16) 1928.

The author gives a general summary and his technic of this procedure in some detail. A serious accident was not encountered in more than 5,000 injections. The best solutions for this purpose are sodium salicylate, quinine and red mercuric iodide. The injections produce a chemical reaction (venitis), leading to obliteration of the lumen and disappearance of functional disturbances associated with varicosities.

ERYSIPELAS: VIII. BACTERIAL ALLERGY TO STREPTOCOCCUS ERYSIPELATIS IN RECURRENT ERYSIPELAS. K. E. BIRKHAUG, J. A. M. A. **90**:1997 (June 23) 1928.

Birkhaug noted six persons who developed erysipelas-like eruptions while undergoing active immunization against recurrent erysipelas with *Streptococcus erysipelatis* toxin-vaccine. The eruption developed in about twelve hours after the intramuscular injections. The method of active immunization proved successful. In some persons with recurrent erysipelas the organism was found in the nasopharynx but was absent from the cutaneous areas. Birkhaug is of the opinion that this observation indicates a state of allergy to the products of *Streptococcus erysipelatis,* and explains those two cases in which the recurrent attacks are limited to previously affected (presumably sensitized) areas.

PRIMARY SARCOMA OF THE LOWER LIP. J. V. FALISI, J. A. M. A. **90**:2015 (June 23) 1928.

The author collected reports of fourteen cases of this condition from the literature, some of which he regarded as doubtful. His own patient was a man, aged 35, in whom the growth appeared in a fissure in the lower lip. Radium and roentgen-ray therapy failed. Necropsy revealed metastasis in the lung.

MICHAEL, Houston, Texas.

ETIOLOGY OF OROYA FEVER. X. COMPARATIVE STUDIES OF DIFFERENT STRAINS OF BARTONELLA BACILLIFORMIS, WITH SPECIAL REFERENCE TO THE RELATIONSHIP BETWEEN THE CLINICAL TYPES OF CARRION'S DISEASE AND THE VIRULENCE OF THE INFECTING ORGANISM. H. NOGUCHI, J. Exper. Med. **47**:219, 1928. XI. COMPARISON OF BARTONELLA BACILLIFORMIS AND BARTONELLA MURIS. CULTIVATION OF BACTERIUM MURIUM, N. SP. H. NOGUCHI, ibid., p. 235.

Nine strains of *Bartonella bacilliformis* were isolated from twelve specimens of blood in verrugous cases, the strains differing only slightly in dark ground examination, but varying more in the stained specimen. The virulence of the strains for monkeys was strikingly variable, most of the virulent strains being derived from severe cases, while some of the strains from benign cases were nonpathogenic.

In the inoculation experiments, local verruga was produced by culture, but no lesions were produced by the corresponding specimens from human blood.

Bartonella muris appeared only in the blood of splenectomized rats and mice; it was not possible to transmit this organism to normal animals. The organisms studied, *Bartonella bacilliformis* and *Grahamella talpae* have individual morphologic characteristics.

STUDIES ON THE INACTIVATION OF VACCINE VIRUS AND THE ACTION OF SUBSTANCES UPON THE INFECTING POWER OF THE INACTIVATED VIRUS. F. D. REYNALS, J. Exper. Med. **47**:389, 1928.

Vaccine virus was found to be more susceptible to chloroform than to ether, toluene, 95 per cent alcohol and acetone. After the virus had been thoroughly chloroformed, it was not possible to reactivate it, so that small quantities would cause an eruption.

STUDIES IN THE PHYSIOLOGICAL ACTION OF HEMATOPORPHYRIN. H. SMETANA, J. Exper. Med. **47**:593, 1928.

In a series of interesting experiments, it was found that white mice were not sensitized to light by feeding on hematoporphyrin, but that when they were stained a blue-black they were immune to the effect of light if hematoporphyrin was injected. The effect of sunlight on the mesentery and intestine of an animal

into which hematoporphyrin had been injected was the same as when the skin was exposed.

In a parabiotic experiment, the blood of one unexposed animal did not protect the exposed animal from the effects of light, these effects in all the animals given injections and exposed to light being similar to traumatic shock. The blood pressure fell to a low level, the temperature was lowered, the venous blood became poor in oxygen and rich in carbon dioxide, and the respirations later were deep and irregular.

The experimental observations did not elucidate the nature of the manner in which these effects were produced.

RECIPROCAL EFFECTS OF CONCOMITANT INFECTIONS. I. THE INFLUENCE OF VACCINIA ON THE REACTION TO INFECTION WITH EXPERIMENTAL SYPHILIS. L. PEARCE, J. Exper. Med. **47**:611, 1928.

Intracutaneous inoculation with vaccine virus into the body of a rabbit at the same time as an intratesticular inoculation with *Spirochaeta pallida* was made resulted in an extremely severe syphilitic infection owing to the disturbance of the host's resistance.

THE RÔLE OF CLASMATOCYTES AND CONNECTIVE TISSUE CELLS IN NONSPECIFIC CUTANEOUS IMMUNITY TO STAPHYLOCOCCUS. S. O. FREEDLANDER and J. A. TOOMEY, J. Exper. Med. **47**:663, 1928.

Broth compresses applied for forty-eight hours before inoculation with *Staphylococcus aureus* produced a local, nonspecific protection which lasted for at least twenty-four hours after its removal. Definite histologic changes were produced: edema, proliferation of clasmatocytes and exudation of polymorphonuclear and small mononuclear cells with thickening of the epidermis. The bacteria were early destroyed by the clasmatocytes, and the fibroblasts rapidly walled off the lesion, resulting in a small localized abscess followed by rapid healing.

JAMIESON, Detroit.

GASTRIC SECRETION AND OTHER DIGESTIVE FACTORS IN ROSACEA. S. R. EASTWOOD, Brit. J. Dermat. **40**:91 (March) and 148 (April) 1928.

Eastwood, in a detailed article with numerous citations from the literature, discusses the subject of rosacea from the historical, ophthalmologic and digestive point of view, the latter discussion comprising a survey of the subject on the basis of the author's observations and cases reported in the literature. Fractional test meals given to fifty patients with rosacea showed low secretory curves in about half of the cases. Hydrochloric acid had a good effect in treatment over a wider range of cases than is accounted for by the low curves. Some digestive disturbances were found in 84 per cent of the cases fully studied. Whatever the type of disturbance, effective relief from it has been accompanied by relief from the rosacea. Excess of carbohydrate in the diet was found fairly constantly. The blood pressure was found to be lower than in healthy subjects. Focal sepsis appears to be a factor in etiology or in maintaining rosacea when developed. An appendix with detailed case reports of forty-six cases follows the article. Sixty references are cited in the bibliography.

FLUORESCENCE, PARTICULARLY IN DERMATOLOGY. H. GOODMAN, Brit. J. Dermat. **40**:105 (March) 1928.

Goodman discusses the fluorescence of the skin and its appendages in health and disease, using the air-cooled mercury vapor arc in quartz as a source of ultraviolet light and a new filter which permits the passage of such light to 2,400 angstrom units and yet bars the visible radiation with the exception of a modicum of the visible violet. He records the appearance of the diseased skin in numerous cutaneous conditions when viewed under fluorescence.

AN EXPERIMENTAL STUDY OF THE PITYROSPORON OF MALASSEZ: ITS MORPHOLOGY, CULTIVATION AND PATHOGENICITY. J. M. H. MACLEOD and G. B. DOWLING, Brit. J. Dermat. **40**:139 (April) 1928.

The authors discuss the morphologic and cultural characteristics, including the sugar reactions and a classification, of the pityrosporon of Malassez. The pathogenicity of the organism and its presence in pityriasis capitis and seborrheic dermatitis is discussed, with experiments in which the skin was inoculated to note whether this would cause lesions similar to those generally designated as seborrheic dermatitis. Experimentally, it did not prove difficult to produce in every case a condition clinically indistinguishable from seborrheic dermatitis, whether the organism was introduced by inoculation or scarification. The authors conclude that seborrheic dermatitis, of whatever type, is a pure fungus infection with the pityrosporon of Malassez. They also feel that the organism is a not uncommon cause of anal pruritus and of scrotal and inguinocrural dermatitis.

LICHEN PLANUS OF THE TONSILS. M. S. THOMSON, Brit. J. Dermat. **40**:191 (May) 1928.

A case is reported in a married woman, aged 33, who presented lesions of lichen planus on both tonsils, in association with typical areas of hypertrophic lichen planus on the neck, scalp and left forearm. She was subsequently seen with a frambesiform syphilid on the sites of the old lichen planus lesions on the skin.

ERYTHEMA ELEVATUM DIUTINUM. H. J. TEMPLETON, Brit. J. Dermat. **40**:193 (May) 1928.

A brief review of the literature regarding the proper classification of erythema elevatum diutinum precedes the report of the case which Templeton presents as being clinically erythema elevatum diutinum of the Bury type, but which histologically is typical of granuloma annulare. The author's case occurred in a white woman, aged 20, who presented a firm, thickened plaque embedded in the skin over the dorsal surface of the proximal joint of the fourth finger. It was slightly nodular and sharply defined, and was diagnosed clinically as erythema elevatum diutinum. A microscopic description and a photomicrograph accompany the article. A photograph of the lesion on the finger is also presented.

DRESSED KID-SKIN MOULAGES: A NEW TECHNIQUE FOR THE COLORED PORTRAYAL OF SKIN-LESIONS. N. TOOMEY, Brit. J. Dermat. **40**:199 (May) 1928.

A technic for the making of dressed kid-skin moulages is described in detail by the author. He states that the dressed kid-skin moulage is lighter, cheaper and quicker to make, and is not subject to being broken by trauma or melted by heat as is the wax moulage.

WIEN, Chicago.

CULTURES, PREPARATIONS AND CASES ILLUSTRATING THE MORPHOLOGY, CULTURAL CHARACTERISTICS, AND PATHOGENICITY OF THE SPORE OF MALASSEZ. J. M. H. MACLEOD and G. B. DOWLING, Proc. Roy. Soc. Med. **21**:39, 1928.

The authors grew the organism in pure culture on artificial mediums and produced experimentally clinical seborrheic dermatitis. They classify *Pityrosporon* among the *Oosporaceae* order of the fungi imperfecti, and say that it is a yeast-like fungus related to *Cryptococcus, Monilia, Saccharomyces,* etc. It differs from *Monilia* in that the spores are pleomorphic while those of *Monilia* are uniform, ovoid or lemon-shaped, and it is about three quarters the size of *Monilia.* Preparations from cultures also differ. In *Pityrosporon,* mycelium is absent in solid

mediums and abundant in fluid mediums in the form of thin, delicate, nonseptate threads. In *Monilia*, mycelium is present, but it is scanty and thick in solid mediums and absent in fluid mediums. Experimentally, patients with a normal skin responded to implantation of the spore of Malassez in a constant way by the development of a group of follicular papules within twenty-four hours. The little eruption lasts about ten days to a fortnight, and then disappears. Some seborrheic subjects developed a widespread irritable patch, while others responded to implantation in the same manner as normal persons do. The primary lesion was always the group of follicular papules.

These observations appear to prove that seborrheic dermatitis of any type is a pure fungus infection with the spore of Malassez. The organism flourishes — to a certain extent like other related fungi — under conditions that favor the development of warmth, moisture and, particularly, seborrhea, though the chemical alteration in the sebaceous and sweat secretion that provides the suitable culture medium is unknown. Seborrheic dermatitis or spore of Malessez infection is therefore found most commonly in subjects with moist and greasy skins, and on those subjects in situations which favor multiplication of the organism, e. g., the infrequently washed scalp, the presternal and interscapular regions, the axillae and intertriginous folds generally. It is not improbable that several conditions not usually regarded as related to seborrheic dermatitis are also caused by the fungus; for example, several of the common types of pruritis ani, scrotal and inguinoscrotal dermatitis and also the acute follicular eruptions which are met with in hot weather and in stokers and others exposed for long periods to high temperatures, and which are possibly identical with the tropical prickly heat.

GUY, Pittsburgh.

THE GENESIS OF MELANIN AND CUTANEOUS FERMENTS. L. H. DEJUST, Ann. de dermat. et syph. **9**:241 (April) 1928.

This article contains a detailed discussion of the biochemistry of cutaneous pigmentation, with particular regard to the production of melanin and to the presence in the skin of oxydases concerned in the formation of pigment. The term melanin is used in a rather loose manner. There is a melanin which can be produced synthetically by the oxidation of tyrosine by tyrosinase. Other phenolic amino-acids give a dark color when acted on by oxydases. The latter products have not received detailed study. They are often confounded with melanin derived from tyrosine.

The pathogenesis of pigmentation in suprarenal disease is not completely elucidated. Bloch's hypothesis that the chromogenic substance is of the nature of epinephrine (two phenol groups) is acceptable, but still an hypothesis. The ferment which acts on this pigment precursor is probably analogous or identical with tyrosinase.

A factor of great importance is the reaction of the medium. Pigment production is favored by an alkaline medium. As to the whole subject of cutaneous pigmentation, one fact is certain: the skin contains ferments for the production of pigment from chromogenic substances. Technical difficulties at present prevent the complete elucidation of this problem.

TRAUMATIC ALOPECIA AREATA. F. MOUTIER and P. LEGRAIN, Ann. de dermat. et syph. **9**:268 (April) 1928.

In discussing briefly the etiologic theories of this disease, the authors ask whether there is a true traumatic alopecia areata. In answer, they report three personal cases occurring after gunshot wounds of the cranium and forty-four compiled cases which were reported during the war. These cases show that alopecia areata follows, though rarely, trauma of the skull. The disease appears in from one to two months after the injury.

RESEARCH UPON THE PATHOGENESIS OF ALOPECIA AREATA. A. LEVY-FRANCKEL and E. JUSTER, Ann. de dermat. et syph. **9**:285 (April) 1928.

The authors' work was directed essentially toward ascertaining the mechanism of the production of the disease and not its causes. They have investigated the autonomic nervous system and endocrine gland function in patients with this disease. In a considerable number of cases vasomotor disturbances and modifications of the oculocardiac, pilomotor and nasofacial reflexes were found. The basal metabolism was increased in eighteen cases and decreased in five. Gonadal and other endocrine symptoms were encountered with great frequency. Dermatoscopic examinations showed arteriolar spasm and diminution of capillaries. From these observations, the authors see in alopecia areata a disorder in which angiospasm is a fundamental factor. In some cases, vasoconstriction is the only phenomenon encountered; in others, it is associated with symptoms of sympathetic or endocrinous origin. The authors conceive of two varieties of alopecia areata; the vasculosympathetic, with normal basal metabolism, and the type that is consecutive to endocrinous disturbances, with abnormal basal metabolism.

SCHAMBERG'S DISEASE. W. DUBREUILH, Ann. de dermat. et syph. **9**:337 (May) 1928.

The author adds four personal cases of this disease to the fourteen cases recently collected by Templeton. The case reports are brief, containing only a morphologic description. A short historical review, histologic investigations and differential diagnosis complete the article.

HYPOSTATIC SUPRAMALLEOLAR CYANOSIS: ITS DIFFERENTIATION FROM OTHER LOCAL CYANOSES. G. DELATER and R. HUGEL, Ann. de dermat. et syph. **9**:344 (May) 1928.

Delater and Hugel present a valuable detailed study of a disorder which has occupied a prominent position in recent French dermatologic literature.

This condition is characterized by a violaceous tinge of the lower legs, with, in some cases, a reticulated or spotted pattern of deeper hue on the affected part. Close examination reveals numerous violaceous telangiectases. Nearly always a deeply colored placard marks the posterior external surface of the lower part of the legs. The disorder is always bilateral. It is accompanied by pain, fatigue and sensitivity to cold. The affected parts are somewhat swollen, and often the leg assumes a cylindric shape.

Objective and subjective symptoms are improved by a position which favors the venous circulation. Capillaroscopic observations revealed obliteration of the normal interpapillary depressions, abnormal capillary forms, dilatation of the subpapillary veins and peristaltic spasms of these vessels in some cases. These observations occasioned the deduction that the cyanotic color is due to an encumbrance of the circulation based on an incoordination and insufficiency of the motor function of the venules.

Histologic study revealed dilatation of the papillary and subpapillary vessels, obliteration of the papillae and collections of dilated vessels about the hair follicles. General examination of the patients disclosed some evidence of neurovegetative and endocrinous dysfunction. The disorder appears almost exclusively in young girls and may disappear after marriage or childbirth.

Diagnostically, the disease must be separated from local cyanosis due to tegumental vascular disturbances (erythrosis, Bazin's disease) and local cyanoses of vascular origin (arterial thrombosis, Raynaud's disease, thrombo-angiitis obliterans, etc.). The foregoing conditions are paroxysmal, affect all extremities, lack reticulation or a spotted appearance and are arterial in origin, while the disease under consideration is fundamentally a venous disorder.

Spontaneous cure occurs. Medicinal measures often fail. Among the latter, obliteration of the veins by injections (when varices are present), rest, physiotherapy, vascular gymnastics and roborant measures are indicated.

LUPUS ERYTHEMATOSUS IN NEGROES. P. NOEL, Ann. de dermat. et syph. **9**:372 (May) 1928.

Lupus erythematosus is rare in colored persons. Noel records the occurrence of the disease in a dark skinned Hindoo. Other cases in colored people should be recorded for the light they may shed on the etiology of the disorder.

GENERALIZED VERRUCOSIS (EPIDERMOPLASIA VERRUCIFORMIS). S. A. GLAUBERSOHN, Ann. de dermat. et syph. **9**:378 (May) 1928.

A case of generalized verrucosis, of which only nine cases are on record, is reported. It is a generalized disease in which there are reddish-brown, isolated or grouped, round or polygonal lesions resembling plane warts. Histologically, hyperkeratosis, acanthosis and vacuolized cells in the rete and basal layers are encountered.

MICHAEL, Houston, Texas.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

PENETRATION OF ULTRAVIOLET RAYS THROUGH CLOTHING MATERIALS. C. C. DOZIER and H. MORGAN, Am. J. Physiol. **84**:603 (April 1) 1928.

Dozier and Morgan found that baby flannel, pongee and crêpe de chine filter out the ultraviolet radiations which are antirachitically potent. The small amount of interspace in the baby flannel and the large percentage of ash in the crêpe de chine and the pongee may have influenced their nontransmissibility. Artificial silk and meadow lane materials transmit the ultraviolet radiations which are effective in healing rickets. However, these materials have the largest interspace and the smallest percentage of ash. These facts seem to indicate that there are factors other than the fiber which may influence the transmissibility of ultraviolet radiation through clothing material.

TWO YEARS' EXPERIENCE WITH MALARIA TREATMENT OF GENERAL PARALYSIS. M. A. BAHR and W. L. BRUETSCH, Am. J. Psychiat. **7**:709 (March) 1928.

Bahr and Bruetsch summarize their observations as follows: Of 100 general paralytic patients, treated with malaria, twenty-five were able to leave the hospital. Twelve patients improved to such a degree that they could be trusted in a useful occupation in the hospital. Forty patients were placed in the unimproved group. In thirty-two patients of the latter group, the disease is progressing. In eight instances the disease has remained stationary. Five patients succumbed during the rigors and eighteen died following the malaria. Serologic changes following malarial treatment occurred in both the improved and the unimproved groups. While there was no parallelism between the degree of clinical and serologic improvement, the percentage of the serologic improvement, particularly as far as the colloidal gold curve was concerned, was higher in the improved groups. The paretic gold curve was reduced in intensity but remained of the paretic type. The conversion of a paretic curve into a true syphilitic one was an exception.

BISMUTH TREATMENT OF SYPHILIS. S. NICOLAU and M. BLUMENTAL, Ann. de mal. ven. **23**:161 (March) 1928.

To the three reported cases of syphilitic reinfection in patients whose first infection had been successfully treated with bismuth exclusively, Nicolau and Blumental add another case and conclude that the four cases prove that bismuth alone is capable of effecting a rapid and even abortive cure of syphilis.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, Jan. 18, 1928

F. E. SENEAR, M.D., *President, in the Chair*

URTICARIA PIGMENTOSA. Presented by DR. WAUGH.

A single woman, aged 51, had a disorder of twelve years' duration. She said that the brownish-red, maculopapular eruption first appeared on the face, neck and arms, then on the lower extremities, and subsequently a few spots were noticed on the body. The lesions were chiefly the size of a split pea, many of them were dark red, and those on the face showed telangiectasia. They were said to become more noticeable at the menstrual periods. There was no itching unless she became warm. In some areas, the skin was almost completely involved in the eruption.

DISCUSSION

DR. OLIVER, DR. FOERSTER and DR. ENGMAN concurred in the diagnosis.

DR. EBERT: The material was fixed in Zenker's solution, and the stain for mast cells was unsatisfactory. The only thing we could observe was a round cell infiltrate about the vessels. Dr. Waugh had to leave, but he asked me to state that the patient has been under observation and has been given various types of medication, without improvement. The lesions seem more widespread than formerly.

DR. ORMSBY: I think the absence of mast cells is not important in the acquired cases of this disorder.

A CASE FOR DIAGNOSIS (POIKILODERMA?). Presented by DR. ORMSBY.

A Polish woman, aged 48, who had been in America for twenty-one years had a disorder of thirty-five years' duration. The first change noted was a rough, chapped condition, beginning on the knees when she was 10 years of age. This gradually spread upward and in three years invaded the thighs and trunk. During the next two years, the upper extremities became involved. During the next five years, nodular lesions appeared in various areas. The skin became red and subsequently scaling ensued. Fourteen years after the beginning of this condition, a course of salt baths was taken; the nodular lesions disappeared and the entire skin improved and remained in a better condition for a year. For the past ten years, nodules had appeared from time to time on the thighs and arms, and the scaling and wrinkling had increased. The face became involved four months before presentation. Itching and burning sensations had been present in varying degrees.

When the patient was presented, the eruption was generalized and exhibited chiefly as wrinkled, scaling, telangiectatic and atrophic patches of varying dimensions. In addition, there were thickened, scale covered, pale red patches and superficial nodules. Over the breasts, on the arms, particularly on the extensor and internal surfaces, over the hips and buttocks there were large patches in which the skin was wrinkled, atrophic and telangiectatic. In these areas, red (telangiectatic) lines surrounded rhomboidal white areas giving a striking appearance. The individual white areas measured 3 by 5 mm. each encircled by a network of vessels. A healed radiodermatitis was suggested, but the resemblance was not striking. Only a small amount of pigmentation was seen. The thickened scaling patches were situated chiefly on the abdomen and thighs. On one thigh near the knee were two rings of superficial pale

red scaling nodules. On the face there was scaling and slightly reddened lesions, varying from the size of a pea to that of a bean. Moderate scaling was also present on the scalp. The palms, soles and mucous membranes did not show any changes.

DISCUSSION

DR. ENGMAN: I thought it was a case of poikiloderma.

DR. ZEISLER: At a distance there was a striking resemblance to a skin that had been treated by roentgen-ray, with marked atrophy and telangiectasia. I agree with Dr. Engman in the diagnosis of poikiloderma.

DR. LIEBERTHAL: I agree with the diagnosis of Dr. Engman, although pigmentation is absent, which could have been expected after the long duration of the disease.

DR. FOERSTER: In the diagnostic approach to this case it is important to note that the woman had a decidedly ichthyotic type of skin, because lesions often are considerably modified when occurring in that type of skin. If we can think of the cutaneous condition in this patient without the modifying influence exerted by ichthyosis, the diagnosis of Brocq's erythrodermie pityriasique en plaques should be given primary consideration. The patchy character of the lesions, the long duration of the disorder, and the extensive involvement I think would all speak for an erythroderma as a possibility or, rather, a probability. I would not like to see the case considered as an instance of poikiloderma atrophicans vasculare. For one thing, as Dr. Lieberthal has pointed out, there is no pigmentation, which I believe should be held as an essential feature in the diagnosis of poikiloderma. It is true that there is a somewhat telangiectatic type of mottling over the breasts, but this is limited in extent and is not present in any other area. There is no atrophy such as we expect to find in scleroderma of long duration, of which we might consider poikiloderma an end-stage in some instances. The patient complains of itching that is worse in the winter months, as is observed by persons, particularly in the Great Lakes region, who have a dry or an ichthyotic type of skin.

DR. WILE: I was impressed with the possibility Dr. Harry R. Foerster suggested that we might have to think of the telangiectatic type of erythematous lupus, which is difficult to rule out. I think this diagnosis should be given some consideration.

DR. ORMSBY: I do not believe that we have seen a large enough number of patients with poikiloderma to have a definite picture of that disorder. It is possible that some of the cases could be examples of that disease that did not exhibit all of the described features. The first case shown here was presented by myself and recognized by Dr. Foerster. That patient's lesions resembled healed radiodermatitis more than those of this patient. The fact that the lesions here resemble lupus erythematosus is in favor of poikiloderma, for some of the cases recorded were at first thought to be that disorder. Taking into consideration the areas of telangiectasia and of distinct atrophy, the long duration and some other characteristics, I think we should first consider poikiloderma, but I believe the case will have to be studied further before the diagnosis can be settled.

DR. HARRY R. FOERSTER: Some years ago, at the annual meeting of this Society, we presented an elderly man who had a condition diagnosed as a poikiloderma. There was little pigmentation in the lesions, a point commented on. Dr. Ormsby suggested the possibility of lupus erythematosus in that case, which I think was in many respects similar to this one.

A CASE FOR DIAGNOSIS. Presented by DR. OLIVER.

A child, aged 6, had a disorder of two years' duration. Two years before presentation, a plaster cast was applied to the right lower leg for a condition

diagnosed as rheumatism. Following the removal of the cast, an eruption developed which subsequently involved both lower extremities and the back. Wassermann tests of the blood of both the child and the parents were negative. A culture was negative. Examination of the blood showed 2,280,000 red blood cells and a slight leukocytosis.

The patient had received small doses of neoarsphenamine and general quartz light treatment, and a mild ammoniated mercury ointment had been used locally.

The patient was a poorly nourished, anemic appearing child, who had a number of ulcers on the sides of the lower portion of the right leg and three on the lower portion of the left leg. There was also one on the upper portion of the right arm and another on the back. These ulcers were shallow and fairly cleancut, with slightly undermined edges. The lesions were irregular in shape and varied in size from that of a dime to that of half a dollar.

DISCUSSION

DR. ZEISLER: I believe that two conditions should be considered: tuberculosis of the scrofulous type and hereditary syphilis.

DR. MITCHELL: I agree that the lesions had a tuberculous appearance.

DR. OLIVER: I think it is a case of tuberculosis. The roentgenograms of the lungs show an almost distinct pulmonary tuberculosis, and the Wassermann reaction of the parents and other members of the family has been negative throughout.

DR. ORMSBY: I examined this patient two years ago. At the time of examination, there was an eruption on the face and extensor surface of the forearms. The lesions consisted of slightly elevated, smooth nodules, some the size of a match-head, others larger, together with numerous erythematous and hyperpigmented relics and some scars. At that time, the condition was of one year's duration. The mother said that occasionally pus discharged from the lesions. There were no subjective symptoms and the Pirquet test was negative. It was thought that the lesions were tuberculids. In view of the present condition, this history is of some interest.

DR. FOERSTER: One of the lesions on the side of the trunk showed scar formation with small ulcers in the scar. I think this is of importance for diagnosis. In addition, on the knee and on the lower part of the thigh there were follicular lesions with a tendency to central necrosis. My impression is that of a mixture of papulonecrotic tuberculid and lichenoid tuberculosis.

ERYTHEMA INDURATUM. Presented by DR. ORMSBY.

A girl, aged 19, presented a disorder which had been present for five and one-half months, which resembled certain cases recently discussed in the foreign literature under the titles of lupus pernio and sarcoid.

The first change noted by the patient was an enlargement of the left great toe. Shortly after this, a few deep "lumps" appeared in the right calf. Three months later, some nodules appeared on the right sole. New "lumps" continued to develop on the calf. None had disappeared. All the toes of the left foot had recently become painful.

On presentation, it was found that the left great and second toes were bluish-red and much enlarged. They were not tender on motion or pressure. There were two deep, tender nodules the size of a pea on the ball of the foot. On the right calf, in the mesial and posterior portions of its upper third, there was an irregular, circular group of firm, bluish-red, deeply situated, painless nodules the size of a hazelnut. In the center of the area, there were pigmented scars. Significant observations were not made during the general examination. The Wassermann reaction was negative.

DISCUSSION

DR. MITCHELL: The only impression I had was that of a combination of erythema induratum and nodosum; in other words, a bacterial embolic process of some kind, possibly tuberculous.

DR. ENGMAN: I think this type of case means a great deal in understanding a large group of diseases. It seems to me this patient is a member of a group that I have seen and observed in several instances; at any time in life the members of this group may have a *Streptococcus hemolyticus* infection associated with the tonsils or something else, then develop slowly a mitral lesion, and within the course of years may have an organic mitral lesion of the heart. This mitral lesion is the habitat of certain strains of streptococci which produce cutaneous symptoms, among them deep, nodular growths such as those seen in this case. I would want a thorough hospital study made of the case, with many blood cultures and careful readings of the temperature. The mitral lesion is not well shown in some instances, particularly in young persons. I have seen lesions thirty years after the original rheumatic infection, occurring on the skin, associated even with gangrene on the fingertips, and giving the whole picture of an obscure streptococcus infection. I have never seen *Streptococcus viridans* cause lesions such as this, but some strain of the hemolyticus is responsible for similar ones.

DR. WILE: I had much the same impression as Dr. Engman, that these were embolic lesions. I did not consider endocarditis as thoroughly as he did, but I think that an extremely interesting suggestion. I thought there might be a remote possibility that these were lesions of erythema induratum, but that we were still dealing with embolic lesions.

DR. STOOKEY: I thought it was an embolic condition, with tubercle bacilli.

DR. ORMSBY: I think the chief interest in this case lies in the fact that during the last few years European physicians have studied lupus pernio and sarcoid extensively, and they have been classifying these conditions together. This is one of the cases that they would probably classify under that head. The disorder probably is embolic, as suggested by Dr. Engman, but it appears to me that the micro-organism that is inducing the lesions is *B. tuberculosis* rather than a streptococcus. It is rather odd that the nodules are distributed so largely on one side, but later this may change. In view of this feature, syphilis was considered, but was ruled out by a negative complement-fixation test.

DR. FOERSTER: Does not the slowing of the circulation favor the localization of organisms in the cyanotic area?

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR and DR. WIEN.

R. S., aged 6 years, an American girl of Italian extraction, developed a growth the size of a hazelnut on the front of the neck eight months prior to presentation. A physician lanced the lesion and evacuated a quantity of pus. Since then there had been spontaneous drainage at intervals until two months before presentation, when the tumor was again incised, scraped and burned.

When first seen a month before presentation, the lesion was a slightly tender, nonpainful tumor with a bluish tint, the size of a hazelnut, and was capped with a hemorrhagic bulla and situated over the cricoid cartilage.

At the time of presentation, there was a thin, atrophic, slate-colored lesion about 1 cm. in diameter in its place.

DISCUSSION

DR. ORMSBY: I have seen several of these discharging sinuses, both in children and in adults, but chiefly in children, and they have all exhibited about this type of lesion with a discharging area attached to the cartilage. I have considered them of embryonic origin. They are difficult to treat, for they frequently recur even following surgical removal.

DR. SENEAR: I have seen three of these cases within the last six months, and I have the same idea as that expressed by Dr. Ormsby.

A CASE FOR DIAGNOSIS. Presented by DR. WIEN.

H. S., a man, aged 31, first noticed an eruption on his neck in October, 1926, and by May, 1927, it had involved the nose, cheeks and the back of the hands. It was accompanied by moderate itching. The eruption was made up of reddish-brown papules, single and grouped, the size of a pea, scattered over the neck, face, nose and ears, with similar lesions on the back of the hands. Atrophy was not present. The buccal mucosa was normal except that there were lesions of Fordyce's disease.

DISCUSSION

DR. LIEBERTHAL: I had the impression that the condition was one of lupus erythematosus. In this diagnosis I was guided especially by the lesions on the auricles.

DR. H. R. FOERSTER: I considered the lesions on the ears and back of the hands lupus erythematosus, and the facial lesions as possibly being lupus vulgaris erythematoides on account of their nodular, squamous character.

DR. WILE: I was impressed with the same thought Dr. Foerster has just expressed until I looked at the hands, but I think the whole picture may be explained as one of lupus erythematosus disseminatus. On glass pressure, the lesions did not show any particularly yellowish tinge, but seemed for the most part to disappear.

DR. ZEISLER: I thought this was a case of subacute disseminated erythematous lupus.

DR. SENEAR: I had the same idea that Dr. Foerster expressed, that we would have to rule out erythematous lupus.

DR. WIEN: The patient was first seen two weeks ago, and at that time the eruption was much redder than at present. The bulbous portion of the nose was the seat of a plaquelike erythema. Telangiectatic lesions were not prominent. I thought the diagnosis rested between lupus erythematosus disseminatus and disseminated miliary lupus, but was impressed by the fact that atrophy was not present. He has received three fractional units of roentgen-ray irradiation and is much improved.

MYCOSIS FUNGOIDES. Presented by DR. OLIVER and DR. ZEISLER.

A white man, aged 50, had had the present eruption at varying intervals for eighteen years. He presented a generalized erythroderma, festooned and in irregularly shaped and sized patches, which covered almost the entire body. At times his skin had been almost free from eruption. There was a slight amount of scaling present, and the involved skin was brick red. The palms and soles were the seat of a hyperkeratosis. On the sides of the trunk, on both forearms, on the forehead, scalp and numerous places on the body were tumors varying in size from a walnut to that of a peach.

The patient had had little roentgen-ray treatment except on the scalp, and said that he had not taken any medication over an extended period.

DISCUSSION

DR. WILE: I wish to know whether the eruption of eighteen years' duration at any time resembled a psoriasis.

DR. OLIVER: From what I could gather it did. When I first saw the man, I thought he had a psoriatic eruption that had been irritated by applications of chrysarobin. This was before I saw the tumor growths. The patient says that the eruptions entirely disappeared at times, which would be a little sug-

gestive of psoriasis, but that the condition had always been accompanied by marked itching, which is against this diagnosis.

DR. WILE: I have seen one case of granuloma fungoides which followed what several competent observers thought was psoriasis. It became very pruritic and lost its peculiar outline, and I wondered whether this case had presented the same symptoms at any time.

DR. ORMSBY: About two months ago, a patient was sent to me who had a condition diagnosed as psoriasis, which had been present for eight or ten years. On examination, I found psoriasiform lesions and multiple tumors of mycosis fungoides. The diagnosis of psoriasis had been made by several physicians, but whether by experts or not, I do not know. Dr. Foerster and I have had experience with one case of parapsoriasis that subsequently developed into mycosis fungoides. I believe that in this as well as in most of the other cases diagnosed early as psoriasis, the psoriasiform lesions are really lesions of mycosis fungoides from the beginning.

DR. WILE: The condition I have in mind is a frank psoriasis, the kind that disappears and returns, with all the earmarks of a true psoriasis. I have seen several cases such as Dr. Ormsby describes.

DR. LIEBERTHAL: This man was in the care of my clinic about three years ago for the present condition. He reported at that time that previous to the development of this, he had suffered for years from scaly patches on the body which disappeared and recurred. I suspected that the latter were psoriatic.

DR. ZEISLER: I have seen a number of cases with psoriasiform lesions in which mycosis developed. In the old literature, there are numerous reports of "psoriasis" developing into mycosis fungoides.

NEVOCARCINOMA. Presented by DR. ORMSBY.

A man, aged 41, presented a disorder of six years' duration. The major portion of the lesions were situated on the left side of the abdomen, but there were a number of dark tumors of various sizes scattered irregularly over the trunk. The first lesion which he noticed was a reddish tumor the size of a lima bean situated in the upper portion of the left quadrant of the abdomen. This was treated with roentgen-ray and later became ulcerated. At the end of six months, small tumors appeared at the margin of the original ulcer. Six months later, the original ulcer was excised and the small tumors treated with the electric needle. Subsequently, several new lesions appeared in the immediate vicinity of the original wound. The process remained largely local until six months before presentation when generalization occurred.

When the patient was presented, there was a linear scar 6 inches long in the lower costal margin. Beneath this was a black, fungating tumor, the size of a lemon, which was papillomatous and exuded pus. Extending in either direction laterally, there were several reddish-brown, firm tumors ranging from the size of a hazelnut to that of a walnut. Scattered in the vicinity and over the trunk in various areas were discrete, bluish-black or pale red nodules and tumors of varying size. There was no evidence of internal involvement.

DISCUSSION

DR. HEDGE: The lesions on the abdomen and left shoulder looked to me like melanosarcoma.

DR. LIEBERTHAL: I agree with the diagnosis of melanosarcoma.

DR. FOERSTER: Are there any visceral lesions now?

DR. ORMSBY: No internal involvement has been discovered as yet. Dr. Wile examined the liver today, and found it normal. The reason I presented the patient was because nevocarcinoma runs such a varied course, and that while the disorder may be quickly fatal, some of these patients live for a long period of time. I have seen the disease run its course to a fatal termination

in eighteen months after the surgical removal or cauterization of a pigmented mole. The present patient has had the lesions for five years and is still in good condition. We have had several other cases of nevocarcinomas that have existed over long periods. At present, the lesions in this case are disseminating rapidly and will probably soon invade the internal organs and terminate fatally. I do not think that anything can be done for this patient, for surgical intervention would probably hasten the dissemination.

DR. HARRY R. FOERSTER: After looking at this patient, Dr. Engman said that he had seen a similar case in which the lesions involuted spontaneously.

DR. OLIVER: I recently saw a patient with what appeared to be a melanotic lesion of the umbilicus. She had three children and was pregnant for the fourth time. Each time there was a great deal of strain and stress on this lesion, and when I saw her it had broken down and was bleeding. The surgeon who referred her to me asked if removal was not indicated. I told him it was, because the lesion was constantly being irritated.

DR. EBERT: One point in this case that I thought was interesting was that according to the history of the patient, he was unaware of any preceding lesion. There was no mole or any such lesion present. At the point of the largest lesion, a small, pinkish spot developed, which was irritated and resulted in ulceration. The other lesions followed.

DR. MITCHELL: Two years ago, I saw a patient who had a brown pigmented mole which had been present all her life, but during the delivery of her child it was cut out because she was told that it would probably cause her death. When I saw her I found that the pigmented portion had by no means been entirely removed. Apparently it had been a benign, hairy, pigmented nevus, but the excision had been poorly performed and had it been a nevocarcinoma, it probably would have caused the patient's death.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR and DR. WIEN.

A woman, aged 26, during a pregnancy four years before presentation developed a slate-colored discoloration of the cheeks, which cleared somewhat following an abortion, but did not disappear entirely. The present disorder started with the appearance of indolent nodules on the thighs, the first appearing three months ago. Since then, new lesions had appeared from time to time. They were hard, subcutaneous nodules varying in size from that of a hickory nut to that of a walnut, and after a few weeks, during which the overlying skin became attached, broke down and discharged pus and necrotic material.

DISCUSSION

DR. HARRY R. FOERSTER: The lesions on the thighs showed a cuplike depression on palpation, which has been described as characteristic of sporotrichosis, and which is also found in one form of tuberculosis. In spite of the negative culture and negative inoculation experiments, I think that tuberculosis and sporotrichosis must both be considered. The peculiar pigmentation of the face might have resulted from applications of cosmetics.

DR. PARKHURST: I agree with Dr. Foerster, but because the patient is a morphine addict, I believe we must consider the possibility of the lesions following hypodermic injections.

DR. LIEBERTHAL: I am inclined to share the opinion of Dr. Parkhurst. I saw a similar case several years ago in a physician who was a morphine addict and who took the drug by injection. The lesions looked the same as those in this case. The discoloration on the face may be due to the same cause.

DR. SENEAR: We originally considered the two conditions Dr. Harry Foerster mentioned, and later we also considered the possibility of the lesions being induced as the result of hypodermic injections. While I realize that we have to discount greatly what a patient of this type says, she was frank in

saying that she used morphine for a year following her operations three years before presentation, but she claims that she has not used it since. She also said that she always made the injections into the arms and never into the thighs. The discoloration of the face developed before any of the surgical operations were performed, and I doubt whether it resulted from the use of the injections.

GRANULOMA PYOGENICUM. Presented by DR. MITCHELL and DR. FINK.

J. B., a man, aged 70, on the plantar surface of the right foot had a lesion the size of a cherry, shaped like a mushroom with a red elevation and surrounded by normal skin. It was said to have followed a nail puncture wound received one week before presentation.

DISCUSSION

DR. OLIVER: I thought it was a rapidly developing granuloma pyogenicum.

DR. ZEISLER: I think we have to be very careful in these cases to eliminate the possibility of a sarcoma.

DR. MITCHELL: When we saw this patient the lesion was bleeding and much larger. The marked improvement shown at presentation is, I think in favor of the condition being granuloma pyogenicum.

DR. FINK: I think the patient received one-half skin unit of roentgen-ray treatment two or three days before presentation. The history of the nail injury and location of the lesion on the ball of the foot makes it appear somewhat like a herniated mass of tissue; that could account for the rapidity of the growth. I had in mind that it developed rather rapidly in comparison with other cases.

DR. STILLIANS: The fact that the condition improved following roentgen-ray treatments would not rule out sarcoma, for some of the sarcomas are susceptible to this treatment. I once clipped off and treated with radium a supposed granuloma pyogenicum, and biopsy revealed sarcoma. It has not recurred in more than ten years.

A CASE FOR DIAGNOSIS. Presented by DR. FINK.

E. O., a man, aged 37, presented bluish, round and oval vascular elevations on the penis, scrotum, inner thighs and trunk, varying in size from that of a pinpoint to that of a pinhead, which were said to have been present since birth or shortly thereafter. The patient was unaware of ever having had a chancre, but the spinal fluid gave a positive Wassermann reaction.

DISCUSSION

DR. FOERSTER: I thought the lesions were multiple capillary ectatic nevi not belonging to the angiokeratoma group.

DR. SENEAR: Dr. Wile had with him slides illustrating the difference between the true angiokeratomas and the multiple angioma of the genitalia. I do not know whether any of you examined them or not.

DR. FINK: This patient has cerebrospinal syphilis, with no obtainable history of infection. I noted that his age as given in the history was much less than the age he looked.

A CASE FOR DIAGNOSIS (LICHEN PLANUS). Presented by DR. S. W. BECKER.

Mrs. C. H., a seamstress, aged 55, had had progressing vitiligo for many years and xanthelasma for ten years. Two daughters also have vitiligo, but four other children did not have it. The patient had always been nervous and inclined to worry. In August, 1927, two months after a severe accident to one of her grandchildren, because of which she was much upset, she noted several "mosquito bites" on the arms and hands. One lesion proximal to the

fourth right fingernail became infected, and this was followed by gradual loss of the nail. There was a sensation of tingling, itching, throbbing and burning which varied in intensity, often keeping her awake at night. Additional lesions appeared on the apposing surfaces of the third and fourth fingers, some of which became the center of a group of lesions, and some of which became crescent-shaped. Only one lesion appeared on the palmar surface of the fourth finger, but she now had what she considered prodromal sensations of itching and tingling of the adjacent palm. In September, 1927, she noted a tingling sensation on the tip of the tongue and found a lesion there. This was followed in November by the discovery of lesions in the right axilla, following the same sensation. In December, 1927, a small group of lesions appeared on the volar surface of the left wrist. She had obtained temporary relief from a lotion which was prescribed by her family physician.

When first seen, a group of small (1.0 by 0.5 cm.), violaceous, angular, flat-topped papules were present on the volar surface of the left wrist. On the apposing and dorsal surfaces of the third and fourth fingers of the right hand, involving the nail bed, were discrete and confluent erythematous papules with a faintly violaceous tinge. The more recent papules were about 0.5 cm. in diameter, were angulated and flat-topped; the older ones were slightly larger and covered with yellowish scales. Practically the entire nail of the fourth finger had been shed and replaced by a thin nail, ridged longitudinally. The lateral portion of the third nail was similarly involved. In the right axilla were two lesions, one similar to the one on the wrist, the second composed of papules in annular configuration, 1 cm. in diameter. On the tip of the tongue was an annular, whitish, opaque lesion with an erythematous center. Farther back on the tongue were three small white macules.

DR. ZEISLER: I thought the lesion in the axilla looked like lichen planus, but if the lesions on the fingers belong to this disorder, they certainly are atypical.

DR. FOERSTER: I thought the lesions were those of lichen planus of the annular type in the axilla and of a peculiar verrucous type on the fingers.

DR. OLIVER: I think the lesions on the fingers were very much like those of the patient we showed last month, a man with lichen planus of the tongue and buccal mucous membrane and lesions on both palms and wrists.

DR. SENEAR: I was interested to see that the lesions on the forearm showed a typical picture of lichen planus. They showed the Wickham's striae particularly well.

DR. BECKER: When we first saw the patient the lesions on the left wrist were typical of lichen planus, but those on the right hand were not. We removed the most recent lesions from the third finger, and the histologic picture is that of lichen planus.

A CASE FOR DIAGNOSIS. Presented by DR. DAVID V. OMENS.

A woman, aged 58, had an eruption which had been present for seven years. She said that the lesions began on the forearms, particularly on the extensor surfaces, later appeared on the buttocks and to a less extent over the dorsal surfaces of the feet. In the beginning, the lesions were few and their increase in number and invasion of new areas had occurred by continuous progression. There had not been subjective sensation. No lesions had disappeared. It was impossible to discover the evolution of the lesions on account of poor observation by the patient. Her general health was not good, but there were no definite pathologic changes.

When the patient was presented, the lesions were situated in the areas noted and consisted of numerous bluish-red, elevated maculopapules which varied in size from that of a match-head to that of a split pea. The major portion were discrete, but some were confluent, forming patches. Slight atrophy was noted in some of the lesions. There were also a few white trophic scars interspersed throughout the areas.

DISCUSSION

DR. PARKHURST: It was my impression that the lesions were sarcoids, and the history stated that they appeared first as nodules.

DR. EBERT: It was my impression that the disorder belonged to that group, and I would classify it between sarcoid and tuberculid. In talking to the patient, I learned that at one time both forearms were equally involved with the bluish-red lesions; one arm has almost cleared up. The lesions on the dorsal surface of the foot are of comparatively recent development.

NOTE: Subsequent to the meeting, a biopsy specimen was taken from the right forearm. The tissue was fixed in alcohol and mounted in paraffin. In sections stained with hematoxylin and eosin, the epidermis was changed very little. Characteristic changes were seen in the corium. At various levels of the reticular portion, there were well defined oval groups of cells with the long axes parallel with the surface.

The central portion of each group was composed of epitheliod cells with an occasional giant cell. Around these was arranged a zone of lymphocytes and cells of connective tissue origin. The histologic picture was that of Boeck's sarcoid.

ERYTHEMA MULTIFORME. Presented by DR. MITCHELL.

A negro, aged 15, was first seen on Jan. 9, 1928, with a severe attack of multiforme erythema limited largely to the buccal mucosa. There had been four attacks during the past two years. The attacks were so severe that the patient was unable to take solid food, and even liquids caused great discomfort. The attacks lasted about three weeks. The general health was excellent, and there was nothing in the history nor in the physical examination to which the disorder could be ascribed. The present attack had been greatly shortened by intravenous injections of calcium chloride.

DISCUSSION

DR. OLIVER: I thought the condition was a recurring multiforme erythema.

DR. ORMSBY: I considered the case to be one of multiforme erythema of the mouth. I saw the man a few days before presentation at the dispensary, and at that time he presented symptoms typical of the recurrent type of the disease in this situation. While these cases with symptoms limited to the mouth are not common, they occasionally occur.

DR. STOOKEY: I saw a similar case of eleven years' duration, which developed in a soldier. These are cases usually associated with lesions on the back of the hands; the diagnosis is always erythema multiforme. The lesions recur, as a rule, every three or four weeks, and there is always a severe infection of the mouth. To me, these factors indicate pemphigus.

DR. MITCHELL: I do not think these cases are particularly rare, and I presented the patient merely to show how relatively common such cases are. We attempted to shorten the attack by giving intravenous injections of calcium chloride, and the boy thought he improved under this therapy. Whether he really did or not, I do not know.

PARAPSORIASIS. Presented by DR. DAVID V. OMENS.

A Jewish pedler, aged 36, had a disorder of sixteen months' duration. The eruption began about the waist and in two months had spread downward over the abdomen and thighs and subsequently over the upper portion of the trunk and arms. Itching had been present at times. He had gained 30 pounds (13.6 Kg.) in weight since the onset of the disease, and there had been no change in his general health.

On examination, the patient was apparently healthy, but quite corpulent. There was a variegated eruption on the covered portions of the body, most marked from the waist to the middle of the legs and on the inner surfaces of the arms. On the lower portion of the abdomen, the anterior and medial surfaces

of the thighs and legs, a definite network could be defined. The bands of this reticulum were made up by fusion of bluish-red macules and brighter red flat papules the size of a pinhead. The papules were less numerous, and many of them were covered with fine scales. The islands of normal skin were 3 or 4 mm. across. On the lateral surfaces of the thighs and legs, the scaling was more marked, and the meshes of the network were more difficult to distinguish. On the buttocks and posterior surfaces of the thighs, the papular elements were more evident, and the background was a diffuse bluish-red. The bright red, scaling papules on the reddish background gave a brighter tone to the inner surfaces of the arms and to the flanks. The upper portion of the trunk and shoulders were only slightly involved.

DISCUSSION

DR. STILLIANS: I thought the condition was parapsoriasis.

DR. ORMSBY: I think the patient presents lesions that more closely resemble parakeratosis variagata than those of any patient previously presented before the Society, but it is not quite typical. I have never seen parapsoriasis of that type in this country, but this case approaches it. I invited Dr. Omens to present the patient because of these interesting features.

DR. FOERSTER: I felt about this case just as Dr. Ormsby does. The reticulation on the upper parts of the arms, particularly about the axilla, resembled lichen annularis. I discussed this feature with Dr. Wile and concluded that the disorder was parapsoriasis.

DR. ORMSBY: This patient's mother had pemphigus two years ago. Dr. Omens treated her with mercurochrome-220 soluble, and she has had no exacerbations for eight months. She is now free from lesions.

SECONDARY SYPHILODERMA (RUPIAL). Presented by DR. ZEISLER and DR. OLIVER.

A man, aged 32, was presented because of an unusual type of secondary syphilis with rupial formation. Examination of the glans showed an unhealed chancre, which was first noticed seven weeks before presentation. On the scalp and forehead were large crusted pustular lesions. On the upper part of the back was an unusually large, single lesion the size of a palm, with characteristic concentric oyster-shell crusting. Small rupial lesions were also present on the extremities.

DISCUSSION

DR. SENEAR: I am sure we are all indebted to Dr. Zeisler for the opportunity of seeing this interesting case.

DR. LIEBERTHAL: We do not see such cases as often at present as we used to soon after the Spanish-American war, and these occurred mostly in soldiers returning from the Philippines who had contracted the disease from natives. In none of the cases seen by me were the lesions as extensive.

DR. STILLIANS: About a year ago, I had a patient, a young woman, who was working here in Chicago and who had many of these ulcers. The Wassermann reaction of her blood was negative at first, but the precipitin test was positive, and she later developed a positive Wassermann reaction. I think the condition usually develops in patients with poor resistance.

DR. BECKER: I saw a patient recently who gave a history of typical rupial lesions fifteen years before presentation. She presented superficial cribriform scars resulting from previous infection and was having another typical attack of rupia. It was striking that the patient should have two similar attacks fifteen years apart.

LICHEN PLANUS LINEARIS. Presented by DR. FINK.

DR. FINK presented a biopsy section from the case of the patient whom he presented at the October, 1927, meeting of the Society as having a lichen planus linearis on the lower extremity. The section showed the following:

The stratum corneum of the epidermis presented a slight amount of hyperplasia plus portions of partially detached nucleated corneal cells. A slight evidence of intracellular edema was present beneath the nucleated corneum. A slight degree of acanthosis was present, which was limited to the area of infiltration in the corium. A moderate elongation of the rete pegs with some clubbing of their deeper extremities appeared in the areas of infiltrated corium. The corium showed a cellular infiltrate sharply limited to the papillary layer. This was composed of round and oblong cells, fairly uniform in size, about half the size of a prickle cell. Areas of perivascular infiltration of the same type of cells were seen about the superficial blood vessels. A perifollicular infiltrate of the same type was visible about several of the hair follicles. A Pappenheim polychrome stain showed the presence of plasma and mast cells in the infiltrate.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Jan. 24, 1928

JOHN E. LANE, M.D., *President*

PAUL E. BECHET, M.D., *Secretary*

ERYTHEMA INDURATUM TREATED WITH GOLD. Presented by DR. BECHET.

A. B., a young girl, said that the eruption had been present for four years. The lesions were characteristic, severe and rather widely distributed on both calves. She had not received any local treatment. Between December 10 and January 21, she was given seven injections of gold and sodium thiosulphate. The lesions have entirely disappeared, leaving only stains.

LUPUS ERYTHEMATOSUS (?) RESISTANT TO TREATMENT WITH A GOLD COMPOUND. Presented by DR. WISE.

Mrs. S. T., aged 34, married, presented a lesion of six years' duration. The eruption consisted of a slight elevated plaque on the right cheek, near the ala of the nose; it measured about 2 by 1½ inches (5 by 3.7 cm.) in diameter, and was roughly oval in shape. The lesion was partly scarred and depressed, as a result of treatment received in Sweden, consisting of refrigeration and radium. The greater part of the lesion presented an elevated, erythematous and somewhat edematous surface, with adherent fine, striated scales. The shell of the right ear exhibited scars which were evidently those of lupus erythematosus and were the result of spontaneous healing. The patient had received intravenously twenty-six successive injections of gold and sodium thiosulphate at intervals of one a week; the dosage ranged from 50 to 100 mg., the last seven being 100 mg. each. There was not the slightest improvement following the injections although the patient did not react unfavorably to the treatment.

DISCUSSION

DR. HIGHMAN: That is a remarkable case to have shown us; nevertheless, I think that perhaps the lesion may not be lupus erythematosus, but tuberculosis of the skin. It is a little deep for lupus erythematosus, and gives signs of infiltration an eighth of an inch (3.17 mm.) thick or more. I should like to see a section of the tissue from the patient studied microscopically. Of course, the condition may be lupus erythematosus, but it does not look like it to me.

DR. KINGSBURY: I do not regard the case as one of lupus erythematosus. The fact that papular lesions are found in the scar tissue does not fit in with that diagnosis. The condition is probably a tuberculous one, and as an initial diagnosis, I would suggest lupus vulgaris.

DR. THRONE: I agree with Dr. Highman and Dr. Kingsbury. In a paper on the use of a gold compound in the treatment of patients with lupus erythematosus, Dr. Calewsky states that some patients who may not respond to one kind of gold preparation will do so if another is given, a gold compound, 4 amino- 2 auro-thiophenol carbonic acid, etc.

DR. MACKEE: I thought it was lupus erythematosus, but I do feel with Dr. Highman, Dr. Kingsbury and others, that it may not be. It may be lupus vulgaris erythematodes, or some other form of tuberculosis. If it is lupus erythematosus, and I think it is, I would not be discouraged because the eruption has not yielded to twenty-six injections, but I would continue the treatment and give two or three 100 mg. doses a week. I have had patients who did not improve until they had received eighty or more injections. I think that Dr. Throne's point of changing the preparation is also a good one, but that should be done cautiously, beginning with small doses. Also, in some of these obstinate cases it is well to stimulate the lesion with mild applications of solid carbon dioxide.

DR. BECHET: There is no doubt that the use of a gold preparation is preeminently the best treatment for patients with lupus erythematosus. The fact that it has failed in this instance might suggest the possibility that the diagnosis was incorrect, and that the case might be lupus vulgaris erythematodes.

DR. LANE: Treatment with the gold preparations seems to have been unsuccessful, and unless it is desirable to experiment further with it, it might be wise to try excision of the whole lesion with the scar.

DR. WISE: I have suspected that the condition might not be lupus erythematosus, but possibly lupus vulgaris. I think that the suggestion of Dr. MacKee is a good one, and I will try it. I will also try to get a small biopsy specimen and will report on the case at the next meeting. The diagnosis of lupus erythematosus was probable, owing to the unmistakable scars of that disease in the shell of the right ear, the lesion apparently having healed spontaneously.

LUPUS ERYTHEMATOSUS (?). Presented by DR. THRONE.

This case was shown by me at the October meeting, and was presented again to show the response to treatment, and to bring up again the question of diagnosis.

The patient had received 0.025 Gm. of a gold compound twice a week since the October meeting. She was remarkably improved. The pigmented lesions on the chin and lower parts of the cheeks were almost entirely gone; the lesion on the nose and adjacent parts of the cheeks was much better. It has been my experience that tuberculous conditions do not respond to gold therapy.

Dr. Fraser and Dr. Highman examined the slide and thought that it showed a tuberculous condition, and suggested that the condition was lupus vulgaris erythematodes. A slide was examined by Professor Ewing, of Cornell, who said that there were no evidences of tuberculosis present.

DISCUSSION

DR. FRASER: When the case was first presented, Dr. Throne had a slide which was examined by several of the members, including Dr. Highman and myself. We did not think the picture justified the histologic diagnosis of lupus erythematosus. Neither Dr. Highman nor myself made a positive diagnosis of tuberculosis. The section was not well prepared. I am still of the opinion that a diagnosis of lupus erythematosus cannot be established from this particular slide.

DR. HIGHMAN: I should like to divide my discussion into two parts: the slides and the patient. As for the patient, as presented, I think it can only be considered a case of telangiectasia that comes after the resolution of lupus erythematosus. I think that Dr. Throne does not regard this patient as satisfactorily

cured yet, and that he is going to continue the treatment, for there is a possibility of reactivation of the lesions. Except for the involvement of the cheeks, the nose itself suggested granulous rubra nasi, and also adenoma sebaceum. I am not advancing these diagnoses seriously, but if it were lupus vulgaris erythematodes, I cannot conceive of tuberculosis having been present and having resolved so soon.

As to the slide, my recollection is substantially like that of Dr. Fraser. I saw a poorly fixed specimen, ragged and nuclear, filled with many epithelioid cells. I could not see enough of the epidermis to determine the characteristics of lupus erythematosus. I saw a great number of epithelioid cells. My impression was that, if anything, it was tuberculosis, but I do not recall making any such arbitrary diagnosis. On the other hand, such a large number of epithelioid cells are not found in lupus erythematosus as a rule, and it is conceivable that the small granular lesions noticed may have some relation to that type of infiltration; but I do not recall having expressed myself as dealing with tuberculosis to the exclusion of anything else.

DR. THRONE: As I recall it, Dr. Highman and Dr. Fraser thought the histologic picture practically excluded lupus erythematosus and suggested lupus vulgaris erythematodes. I presented the case again in order to bring up two points: (1) If possible, to clear the diagnosis for the clinical records in the hospital; (2) to show that the case exhibits clearly the same thing brought out in Dr. Wise's case. This patient did not respond to treatment with a gold preparation until the treatment had been continued over many months. She was started on this therapy on July 22, 1927, and has been under that treatment for practically six months, receiving injections at least twice and sometimes three times a week. Probably one reason for the failure to respond was that she did not tolerate the drug well, and when the injections were increased to more than 25 mg. she had pruritus and an increase of sugar in the blood, so that the treatment had to be discontinued temporarily. Of late she has been getting 25 mg. twice a week, and the improvement has been marked. In presenting the case I stated that Dr. Highman and Dr. Fraser thought the slide showed a tuberculous picture, and suggested that the case was lupus vulgaris erythematodes.

A CASE FOR DIAGNOSIS (ANGIOMA SERPIGINOSUM?). Presented by DR. BECHET.

P. G., a boy, aged 6, had had a grouped unilateral eruption on the left side of the face, consisting mostly of various-sized nodules, topped and surrounded by telangiectatic blood vessel formation of four months' duration. He had been under observation for several months, and the nodules had disappeared, leaving several erythematous patches; all of them contained a delicate network of dilated capillaries. One of the patches near the nose showed distinct atrophy. All of the patches tended to be grouped and annular in distribution. Bright red dots appeared at the periphery of some of the lesions. The biopsy had not proved of much help, the report of the pathologic reading being "chronic inflammatory reaction." There was an infiltration of lymphocytes and connective tissue cells. The epidermis was thin but normal. The small blood vessels were hyperplastic.

DISCUSSION

DR. MALONEY: I am inclined to agree with the diagnosis. It seemed possible, in one of the lesions, to demonstrate telangiectasia and the rather characteristic cayenne-pepper spots of this disease, but in none of the other lesions were these signs present.

DR. HIGHMAN: It is not so easy to fit the case into any of the conventional groups of telangiectasia of the skin—angioma serpiginosum or any other. Angioma serpiginosum may indeed arise from a preexisting telangiectasia, but the picture as present in this patient does not look like angioma serpiginosum or any other condition I have seen. It seems more like a dilatation of the vessels that some-

times persists after the disappearance of all kinds of exudative lesions, notably after sarcoid of Boeck, which resolve spontaneously, leaving a pigmented spot or dilated blood vessels which may or may not disappear. I fancy this case is something of the sort, some persisting past the inflammatory process and leading to telangiectasia which may be permanent.

DR. RULISON: I have no diagnosis to offer, but was much puzzled by the fact that compression did not produce any fading. I cannot conceive of a vascular erythematous condition which would not fade with strong pressure. I think the color effect must in some way be due to pigment rather than to dilated blood vessels.

DR. WISE: I should not think it was angioma serpiginosum. Histologically, there might be an increase of the blood vessels, and clinically there might be a purpura-like telangiectasia persisting after some preceding eruption, but that does not make it angioma serpiginosum. Only a few cases have been described and accepted as angioma serpiginosum. In these, the blood vessels were distinctly visible at a distance and could be partially pressed out. They were usually arranged in tiny rings, and presented, in addition, the cayenne-pepper spots; rings and cayenne-pepper spots were the two chief features. I cannot offer a diagnosis, but it is my impression that since this lesion began as a nodule angioma serpiginosum can be excluded. I must therefore agree with Dr. Highman that this is probably the remains of some preexisting active lesion, or possibly a form of nevus.

DR. MACKEE: I have the same impression that Dr. Highman and Dr. Wise have expressed, namely, that we are dealing with a purpura and erythema remaining after the involution of an inflammatory dermatosis.

DR. BECHET: When I first saw the case, some of the lesions were undoubtedly infiltrated and nodular. All of them were hemorrhagic; the telangiectasia was apparently present from the beginning. I think that what Dr. Wise and Dr. Highman have said might probably prove correct, yet the nodules disappeared rapidly, and the newer lesions which have appeared have not become nodular. They are grouped, telangiectatic, symmetrical, serpiginous, slightly atrophic and hemorrhagic. With these symptoms, the diagnosis of angioma serpiginosum deserves serious consideration, and I am not yet positive that this diagnosis can be eliminated.

PITYRIASIS RUBRA PILARIS. Presented by DR. ELLER.

R. V., a girl, aged 6, from the Post-Graduate Skin Clinic, presented an eruption of about seven weeks' duration, which was first noted about Thanksgiving, 1927. The eruption began on the upper anterior part of the chest in patches consisting of erythema, exfoliation and follicular keratosis; they gradually involved the entire body. The patient was convalescing from a moderately severe case of whooping cough. The eruption seemed to be fading and subjective symptoms were not present, although at first there was a slight itching.

DISCUSSION

DR. BECHET: It is a classic example of the disease, and there is no question as to the diagnosis. I had a similar case in an older boy with a typical Fröhlich's syndrome, and there is no doubt that he was helped by the administration of pituitary extract. Nothing was done locally, yet the eruption disappeared to a great extent. Levin succeeded in curing a patient with pityriasis rubra pilaris associated with hypothyroidism by the administration of thyroid. In a disease of unknown etiology like pityriasis rubra pilaris, it is not amiss to try glandular therapy if an associated endocrine disfunction is clearly noticeable.

DR. WISE: About three years ago, Dr. Abramowitz presented a child similar to this who had well marked pityriasis rubra pilaris; the disease appeared to clear up under endocrine therapy.

DR. THRONE: In the *British Journal of Dermatology and Syphilis*, a few years ago there was an article stating the benefit derived from parathyroid. Since then we have treated several patients at the Skin and Cancer Hospital and the condition in all of them has cleared up.

DR HIGHMAN: I had a patient, a man in the early twenties, who presented what looked like Fröhlich's syndrome and had urticaria. I noticed that the urticarial outbreaks occurred about every four weeks. I gave him ovarian extract and he recovered. This is true. If this is endocrinology, make the most of it.

MYCOSIS FUNGOIDES. Presented by DR. WISE. (From the Skin Clinic of the Post Graduate Hospital.)

R. S., a woman, aged 76, married, presented a widespread and severe eruption of mycosis fungoides of six years' duration. The eruption began on the abdomen, and new lesions rapidly developed, practically over the entire body. When first seen, the eruption consisted of irregularly outlined, round and oval plaques, mostly on the trunk, with well-defined, elevated tumor formations, chiefly on the thighs and the backs of the forearms. These elevated lesions had resolved under roentgen-ray treatment. On presentation, the skin presented an almost uniform dark red and violaceous discoloration, affecting the entire trunk and the greater portion of the lower extremities. On the scalp were several disseminated erythematous plaques. At the time of presentation, the eruption on the thighs and the abdomen resembled dermatitis exfoliativa. The patient suffered from intense and constant pruritus, despite the fact that she was under active roentgen-ray treatment, and increasing dosages of arsenic by intramuscular injection.

TATTOO. SHOWING RESULT OF SELF-TREATMENT. Presented by DR. BECHET.

R. O., an Armenian girl, aged 23, had been captured by the Turks ten years previously, and tattooed with the usual bluish-black trident on the median line of the forehead and the lower lip. She had been unusually successful in her attempts to remove the blemish from the forehead; the resulting scar was superficial, and much of the pigment had disappeared. The method that she used consisted of needle puncture and rubbing in of lemon juice. The lesion on the lip had not been touched.

ACTINOMYCOSIS. Presented by DR. MALONEY.

C. C., a man, aged 29, a stableman, born in Italy, presented an irregular nodular mass, the size of a small hen's egg, on the left cheek just above the angle of the jaw. On the surface of this mass were several pustules and crusts. It had begun six weeks before presentation following treatment of an abscessed tooth. The ray fungus was demonstrated in the secretion and later an examination of a section of tissue confirmed the diagnosis.

EPITHELIOMA OF UPPER EYELID TREATED WITH SUPERSOFT ROENTGEN RAYS. Presented by DR. ELLER.

The patient was a man, aged 45, who presented himself at the Post-Graduate Skin Clinic with a lesion which involved the entire upper right eyelid. The lesion was markedly infiltrated. The eyelid drooped due to the weight of the lesion. Treatment consisted of eight doses of the roentgen ray produced by voltages of 8,000, a Muller tube (made in Berlin) was used, which had a Lindermann glass window permitting wave lengths of 1½ to 2 angstrom units to pass through. Double erythema doses were given at intervals of from three to four weeks. The lesion had entirely disappeared, leaving a soft nonatrophic skin. No extra protection was given the eyeball, and the two ophthalmologists who had the patient under observation did not note any irritation of the eyeball at any time during the treatment or afterward.

DISCUSSION

DR. MALONEY: We are treating a number of patients with basal cell epithelioma with these rays at the University and Bellevue Clinic, with the same good results.

DR. WISE: I would like to know if Dr. Maloney has seen any patient treated with Grenz rays in whom the results are different from those with the ordinary roentgen ray.

DR. MALONEY: Yes, we treat patients with rosacea by general exposure to the Grenz rays, and we have had the condition clear up remarkably in three cases.

ERYTHEMA PERSTANS. Presented by DR. MALONEY.

C. B., a man, aged 32, chauffeur, born in the United States, presented an eruption of ten months' duration on both arms and legs. This eruption was made up of various sized erythematous patches, rather sharply circumscribed in most instances. In some areas several patches had become confluent, forming plaques as large as the palm of the hand. In many of the patches were minute papules, and these lesions were itchy. On the trunk were small pigmented areas, evidently the location of previous lesions.

The patient gave a history of having had similar eruptions at various times during the past ten years.

DISCUSSION

DR. MACKEE: It seems to me that we are dealing with a dermatitis, not an erythema. There are numerous patches of eczema that may have been caused in various ways, but to me they suggest dermatophytosis.

DR. FRASER: I recently saw a similar case, and roentgen-ray treatments in ¼ skin unit doses administered at weekly intervals cleared the lesions.

DR. HIGHMAN: I have had a number of these cases and can understand both Dr. Maloney's and Dr. MacKee's points of view. When I first saw the case in the clinic, it did not have so much the effect of dermatitis as of an erythema. Today I looked at the slide hurriedly, and there are few changes. It is an edema of the epidermis, including the papillary areas, with slight edema in the upper levels of the corium proper. None of these changes in the epidermis are significant of true dermatitis. If it had not been for the edema and a slight infiltration around the blood vessels, I would say that the piece of tissue came as near being normal as skin could well be. Of course, the erythema was accounted for by the dilatation of the vessels. Because of the morphologic as well as the microscopic observations, I should be inclined to consider this an erythema perstans, but that is by no means a final opinion. I will study the case further, and report on it at the next meeting.

DR. LANE: If I had seen the case without any history, my feeling would have been the same as Dr. MacKee's, except that it did not impress me as being epidermophytosis. There is nothing that does not fit in the picture of chronic eczema. One of the lesions is dry and lichenified; the irregular lesions around the neck are of the same character though not so much thickened. Of course these may have been modified by treatment, but in spite of that it seems a rather unusual picture of chronic eczema.

PARAPSORIASIS EN PLAQUE WITH ALOPECIA. Presented by DR. WISE.

M. S., a man, aged 66, had been presented a year previously before the Section of Dermatology of the New York Academy of Medicine as having a case of parapsoriasis en plaque the duration of which had been two and a half years. Since then the eruption had become worse, and the man complained of considerable itching. In addition to this eruption, he had recently developed alopecia areata of the scalp.

DISCUSSION

DR. LANE: There is no doubt about the diagnosis, but I thought the case well worthy of notice. The eruption on the back has a form and distribution remarkably similar to the eruption of pityriasis rosea.

DR. WISE: The only point I would bring up is that the process in this patient shows a certain amount of variation from month to month. The patient has been under observation for two and a half years, and is the grandfather of the physician who referred him. The histologic section confirmed the diagnosis.

KAPOSI'S SARCOMA, WITH UNUSUAL FEATURES. Presented by DR. BECHET.

S. R., a white man, aged 21, stated that three years previously he had noticed on the toes of his right foot several small nodules which grew slowly until seven months previous to presentation, when extension of the disease became rapid. On inspection, a large number of nodules with involvement of the blood vessels were noted on both legs. The lesions varied from a violaceous to blackish-brown color, and had aggregated to form several rather large, papillomatous, verrucous-like patches. Individual hard, rounded, nodules the size of a pea were noted, extending almost to the knee. The lymph nodes in both groins, axillae and cervical region were markedly enlarged. There was a large tumor in the right axilla. The patient's general health had become worse rapidly. A blood count showed 3,670,000 red blood cells and 9,400 white cells. The differential count showed: polymorphonuclears, 67 per cent; lymphocytes, 18 per cent; mononuclears, 9 per cent; transitional, 1 per cent; eosinophils, 5 per cent and hemoglobin content, 78 per cent. The results of the roentgen-ray examination of the chest were negative. The youth of the patient and the rapid tendency to malignancy, as well as the tumor in the axilla, were the features of special interest.

DISCUSSION

DR. HIGHMAN: I think it is a case of Kaposi's sarcoma that is beginning to metastasize. There is edema of the leg, and the inguinal glands are much enlarged, as though they, too, were involved. The tumor in the axilla seems too elastic to be a lymphatic gland. Twelve or fifteen years ago, Gilchrist and Ketron read a paper on Kaposi's sarcoma with reference to malignancy, in which they showed that when the malignant phase was inaugurated the character of the sarcoma was often altered from that of angiofibrotic sarcoma to either spindle cell or small round cell sarcoma. I think that is what is happening in this young man, and that he has not many years ahead of him.

DR. FRASER: I agree with the diagnosis. These cases as a rule are comparatively benign, but when they do become malignant there is a transformation to the round cell type of sarcoma.

DR. WISE: Despite the rather grim outlook for this patient's future, and although Dr. Bechet did not ask for any therapeutic suggestions, I would suggest that the patient be given arsenic in increasing dosage to the point of tolerance, together with filtered roentgen-ray therapy.

DR. BECHET: I am glad to have Dr. Wise's suggestion and will act on it. I presented the case mainly on account of the age of the patient. It is unusual to see the disease in so young a man; it began when he was only 18. The disease is apparently pursuing a malignant course, which is another unusual feature.

MYCOSIS FUNGOIDES. DR. WISE.

I would like to report on the case of mycosis fungoides presented at the preceding meeting, the patient being a man 60 years of age. Some of the lesions were so vague that the diagnosis was doubted by several of the members. I have a section here, showing the histologic structure of mycosis fungoides.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Friday, Feb. 3, 1928

DR. CARROLL S. WRIGHT, *in the Chair*

KERATOSIS BLENNORRHAGICA. Presented by DR. SIDLICK.

J. R., aged 35, had had a skin condition for the past four months. The patient thought that the lesions first appeared on the scalp and later on the forearm, the backs of the hands and the soles of the feet. Some of these showed a yellow, thickened epidermis, and others looked like psoriasis. On close inspection, however, none of the characteristics of psoriasis are present.

The history of arthritis is of interest. In 1920, the patient had a painful left wrist; in 1921 a second attack occurred together with a pain in the right instep. In 1925, he had a third attack involving the right instep. On Jan. 23, 1928, the present attack began, with pain in the right second toe and swelling of the right knee.

DISCUSSION

DR. KLAUDER: I do not subscribe to the diagnosis of keratosis blennorrhagica, for the reason that the lesions are not sufficiently keratotic. Those on the palms and soles certainly bear a considerable resemblance to syphilids. It is logical, however, to consider all the lesions of the same nature, and the other lesions do not resemble those of syphilis; those on the scalp are characteristic of seborrheic eczema, as are those around the perineum. I think the diagnosis of seborrheic eczema would fit all of the lesions better than psoriasis, syphilis, tinea or keratosis blennorrhagica. If one accepts the last diagnosis, one has to divide the process into two diseases.

DR. WEIDMAN: The fact that the patient had arthritis goes a long way toward fortifying the diagnosis as given. I recall my reaction to the first case of keratosis blennorrhagica that I saw. It was shown four or five years ago, and it was surprising to me to note erythema at the margins of the lesions, and at once my own idea of the process changed. I had thought it was a keratosis in the same sense that keratosis senilis is; that is, at the bottom of it a simple vice of keratinization, but in all of the several cases I have seen since then there has been an outstanding element of hyperemia at the borders. The term keratosis is a misnomer; it is really a keratotic dermatitis. I think that was brought out forcibly in a patient shown at the last meeting of the Atlantic Dermatological Conference. In that case, when I first saw the patient in the hospital, the lesions were keratotic, but when the time came to demonstrate the case, the keratoses had disappeared, and the red, inflammatory, infiltrated bases were all that was left. After that experience I can understand how the lesions in this patient could be so-called keratoses blennorrhagica, without the keratotic factor being developed or perhaps altered as a result of treatment.

The lesions on the palms, though, I think present whole hearted acceptance of the diagnosis. They do indeed resemble other things: squamous syphiloderma or a fungous infection. Those little points in the centers of the patches which sometimes contain turbid fluid favor ringworm of the palms, and whereas it may be that this is a case of keratosis blennorrhagica, as supported by certain clinical data, I think continued effort should be made to demonstrate fungus before the diagnosis is made definitely.

DR. SIDLICK: I forgot to mention the Wassermann reaction. At present it is negative, although at one time, three years ago, it was positive. Following treatment it became negative and has remained persistently negative. I have observed the development of these lesions, particularly on the soles of the feet. They usually began with small, deepseated pustules, which ruptured and formed crusts. They did not resemble syphilids, and furthermore, a number of lesions on the forearm have appeared during the past two weeks. While

there is a possibility that they are due to fungi, in exhaustive studies of scrapings from many lesions, I could not find any evidence of fungus.

DR. WRIGHT: It is unfortunate that no one has even been able to demonstrate the gonococcus in lesions of keratosis blennorrhagica. Dr. Keim at the University of Michigan attempted to demonstrate them in a case much more clearcut than this, without success. We therefore have no way of proving whether the condition in a case is keratosis blennorrhagica or not. The members who attended the Atlantic Dermatological Conference may remember the discussion about this point. Many of the lesions in the case presented at that meeting resembled lesions that might have been caused by fungus infection, and the question was raised whether this was due to gonococcus or whether the eruption occurring in patients with gonorrhea was due to a secondary invasion by fungus. I do not think any one can say whether this is a keratosis blennorrhagica or not.

ACANTHOSIS NIGRICANS. Presented by DR. RAPP, from Dr. Klauder's clinic at the Philadelphia General Hospital.

E. T., a colored girl, aged 12, weighing 260 pounds (117.9 Kg.), presented slightly elevated, pigmented, rough lesions around the neck, in the axillae, under both breasts, on the anterior surface of chest and in the interscapular region. On the upper lip there was also some increased pigmentation which spread to both sides of the chin. There were numerous pea-sized patches of pigmentation over the back.

A roentgenogram of the skull showed nothing abnormal. Results of the abdominal examination were entirely negative. The only particular feature of this case, other than the acanthosis, was the extreme obesity for a person 12 years of age.

DISCUSSION

DR. CORSON: I think the case conforms clinically to the diagnosis given. To be positive of the diagnosis, however, I should prefer to see a person who was not laboring under this endocrine dysfunction and who had a white skin.

DR. GREENBAUM: The patient has the papillomatous and the pigmentary disturbances that correspond, in a way, with the condition of acanthosis nigricans. It probably belongs to an abortive form. Because of the obesity, it would tend to strengthen our thoughts concerning endocrine disturbance as a factor in the production of this condition. I would be interested in knowing what the basal metabolism test would show as well as the dextrose tolerance test.

DR. KLAUDER: Results of examination for endocrine disturbance were negative. The patient presented an unusual number of scattered patches of pigmentation for a patient with acanthosis. I think it is the second case presented before the Society in a number of years.

DR. SIDLICK: The diagnosis of acanthosis does not present any difficulty, but it is interesting in regard to possible etiology. It is often maintained that the condition is due to a malignant tumor. Acanthosis in a young child or an adult is also supposed to be due in some cases to adhesions causing disturbances in the nervous system, which in turn cause acanthosis. While perhaps there is some basis for the argument, no one cause seems to explain all the cases of acanthosis. There are many cases on record in which exhaustive studies both before and after death have failed to reveal the presence of a malignant tumor or any mechanical obstructions which would cause a disturbance of the nervous system. The etiology is more interesting than the diagnosis.

LUPUS ERYTHEMATOSUS ACUTUS DISSEMINATUS. Presented by DR. FANNING for DR. BROWN.

L. F., aged 35 years, colored, had a patch on the back of her head seven years before presentation which gradually spread over the head, on to the

face, neck, trunk and arms. For the past year the eruption has been stationary. The patient was in excellent health until one year previous to presentation, and at that time she began to complain of a condition in her rectum. The blood Wassermann reaction was 4 plus with all antigens. She had a moderate secondary anemia. The roentgenogram of the chest was normal, except that the roentgen-ray report shows a syphilitic heart. The condition in her rectum at this time is not fully determined. Biopsies show a thickened mass in the lower part of the rectum which the surgeon has thought possibly malignant.

The blood count is as follows: white blood cells, 8,200; polymorphonuclears, 59 per cent; lymphocytes, 38 per cent; and eosinophils, 35 per cent.

DISCUSSION

DR. WEIDMAN: The blood count is important in the prognosis.

DR. GREENBAUM: I agree with the diagnosis of lupus erythematosus, but do not consider the condition an "acute disseminate" type. There is, of course, the additional condition of ichthyosis on the extremities which must not be confused with lupus erythematosus.

DR. KLAUDER: This is one of the most disseminated types of lupus erythematosus that I have seen for a long time. I believe the appellation "acute disseminate" type is not appropriate for this patient. This term should be applied to patients with constitutional symptoms and fever, who present the characteristic erysipelatous appearance of the face designated by Kaposi as erysipelas perstans faciae. In addition, there is an eruption on the trunk or extremities, frequently pulmonary symptoms and usually a fatal outcome. I think the proper classification of the type presented by this patient is chronic disseminated lupus erythematosus.

DR. GREENBAUM: I have seen at least three varieties of lupus erythematosus that I would classify as "acute disseminate." The exanthematic type, which looks somewhat like erysipelas, is really acute. Then there is the type of fixed lupus erythematosus associated with the development of ten, twenty or thirty lesions on the body that does not correspond, at least clinically, to the lupus erythematosus acutus disseminatus of the facial type. I have also seen a definitely septicemic type characterized by widespread lesions over the entire body, erythematous, some of the lesions bullous, and likewise ending fatally with terminal pneumonia. The present case corresponds to the fixed type, with the development of a few lesions on the upper part of the chest and on the scalp. As I see it, the condition on the legs and arms is largely ichthyotic. This type has a much better prognosis.

DR. WRIGHT: If a gold compound is to be used in this case, I would recommend that treatment be started with small doses, say 10 mg.

DR. CORSON: It would be interesting to note, if this patient is treated with a gold compound, whether any hair grows again on the scalp. At the Atlantic Conference, a case was shown of a woman almost as bald as the one in this case, who had a regrowth of hair after receiving a number of injections of a gold compound.

A CASE FOR DIAGNOSIS. Presented by DR. CROSS for DR. BROWN. (From the Dermatological Wards of the Philadelphia General Hospital.)

A man, A. B., aged 30, was presented about a year ago before this society. There was some question about the diagnosis at that time, although the patient was presented as having a case of tuberculous ulceration of the leg. He is now presented, with additional data.

The patient now presents an extensive ulceration on the right leg of fourteen years' duration, following a barbed wound in the ankle received fourteen years before presentation. Since that time this condition has extended up the leg, and at present there is a linear ulceration with a clean base and an irregular sloping border. The patient had a hard penile lesion in 1921, and a positive

Wassermann reaction, after which he received twenty-two intravenous injections of arsphenamine and about ten intramuscular injections in the hip. Since 1923, the Wassermann reaction has repeatedly been negative.

The roentgenogram shows a thickening of the right tibia and fibula with irregularity of the bone. There is thickening and increased density of almost the entire cortex, evidently a chronic osteomyelitis; also irregularities in the cortex, which suggest syphilis as an etiologic factor. The pathologic report of a section from the border is "chronic inflammation." The patient has had two skin grafts during the past two years, and twelve intravenous injections of 100 mg. each of gold and sodium thiosulphate. Locally, he has had a variety of antiseptic dressings and ultraviolet ray therapy. Inoculation into a guinea-pig was positive on one occasion for the tubercle bacillus.

DISCUSSION

DR. SIDLICK: This patient was admitted to the Philadelphia General Hospital ten days previous to presentation. Since then treatment has consisted merely of spraying the wound with an antiseptic and the application of heat by means of a vacuum bulb. I wish to call attention to the fact that the upper part is almost completely filled in, and there are new granulations all along the base. The history is highly suggestive. The patient has been in a number of hospitals, particularly one in Baltimore, where he remained for a considerable time, and, according to his own statement, the condition was at that time almost entirely healed. The duration of the ulcerations, fourteen years, is highly suggestive that we are dealing with a dermatitis factitia. We have been watching him in the hospital. Under simple treatment, marked improvement has occurred.

DR. KLAUDER: Two patients were presented at a meeting of the American Dermatological Society held in Philadelphia in June, 1926, with the same type of ulceration of the extremities. I do not believe this type of ulceration is tuberculous; it does not conform to any clinical type of tuberculosis. I believe it is an ulceration of which the cause has not yet been demonstrated.

DR. WRIGHT: One observation must be given serious consideration. A bit of the tissue was inoculated into a guinea-pig, and the tubercle bacillus was recovered later from that guinea-pig. It is difficult to explain this fact other than that the tubercle bacillus must have been present in this lesion at some time.

DR. SIDLICK: Histologic study did not reveal tuberculosis. I cannot believe that simple, everyday treatment would improve the ulceration so much if it were tuberculous.

DR. WRIGHT: The patient had a good deal of treatment with a gold compound a year ago, which might possibly have had some effect on a tuberculous process. He had some treatment with neoarsphenamine, which we know in some cases has a beneficial action on tuberculous ulcers. It is possible that the active process may have been eradicated, leaving a chronic ulceration in need of skin grafts to complete the healing.

DR. WEIDMAN: When a patient gives a history of having acquired a local tuberculous infection in one of the southern states, we should remember the cactus spine tubercles reported by Warthin and others at Ann Arbor, in which one of the notorious sequelae is the development of tuberculosis. This man was originally injured by a barbed wire fence. Whether cactus spines were present in the neighborhood or not, further history might reveal. Apparently the trouble did not begin at the bone, and it is not hematogenous; it extended not from the inside out but from the outside in. In a case of this kind we should also inquire into the matter systematically; not along with the idea that the disease extended there hematogenously, but that it was planted there locally. Dr. Allen J. Smith, I remember, used to tell us that the methods of distribution from one part of the body to another were many; how it was

possible that virus could be merely smeared over the surfaces; and how there were superstitions, particularly among the lower class, about the virtues of spittle applied to a lesion to improve it. In this way a person with pulmonary tuberculosis might transmit tuberculosis to an ulcer or other lesion on the skin. I think the question of pulmonary tuberculosis ought to be considered in this case.

As to the definite improvement of tuberculous ulcers, I have seen at least two cases of tuberculosis verrucosa cutis in which the patients were cured by the application of a compound solution of iodine locally as wet dressings, the hypodermic needle being used to squirt the fluid into the sinuses. I think that a compound solution of iodine might be used to advantage in this case.

Mycosis Fungoides and Epidermophytosis. Presented by Dr. Sidlick.

E. G., aged 43 years, presented a skin condition of three months' duration, consisting of circumscribed areas of dermatitis, some dry and some weeping. In addition, he had a vesiculopustular eruption on the soles of the feet, which was due to fungi.

Dr. Weidman reported that the sections from the lesions on the body were suggestive of the premycotic stage of mycosis fungoides.

DISCUSSION

Dr. Corson: I agree with the diagnosis. It is an unusually rapidly developing case, if the history is correct. We generally expect the eczematoid stage to last considerably longer than that before we see localization and infiltration. The biopsy scar appears to have developed a fungating lesion; it looks like more than just exuberant granulation.

Dr. Weidman: I imagine this is the sort of case that often is presented at a number of different dermatologic societies and is commonly regarded as granuloma fungoides. There are reports of cases of Hodgkin's disease and leukemia cutis in which the condition began much like this. I have at present in the laboratory five or six hundred slides from a case that came to necropsy in which the condition proved to be Hodgkin's disease, although it was originally diagnosed, by one of the leading dermatologists, as atypical psoriasis. Finally, the girl developed large lesions on the neck, and it was obvious enough that it was a case of Hodgkin's disease. I think perhaps prior to the development of those little nodules in the biopsy lesion this case was a little early to diagnose unequivocally as granuloma fungoides as against a possible Hodgkin's disease, although according to statistics, of course, the probability is greater that it would turn out to be granuloma fungoides. But dermatologic experience is replete with instances in which the appearance of patients with Hodgkin's disease and leukemia cutis has been the same as that of this patient even in the absence of any enlargement of the lymph nodes externally. It may be a case of retroperitoneal Hodgkin's disease, or the lesions may not make their appearance until the lesions on the skin have been in existence for a long time. I wonder what the blood picture was in this case. I think this development in the biopsy scar strongly supports the diagnosis of granuloma fungoides.

Urticaria Pigmentosa. Presented by Dr. Sidlick.

J. McC., aged 7, white, was admitted to the Philadelphia General Hospital from a charitable institution five days before presentation; consequently, no history is available as to how long the eruption has existed. The patient presents a generalized eruption consisting of pigmented macules, which on the average were 1 cc. in diameter. On stroking, these macules develop into wheal-like lesions.

DISCUSSION

Dr. Weidman: I think that is a good diagnosis; so many of those lesions look like the fading marks of some preexisting lesion, such as impetigo or scabies. I cannot say that I have ever seen a case of urticaria pigmentosa in

which some of the lesions had this finely follicular appearance, and in which a single lesion was comprised of a great many punctate elevations, which do not appear to be urticarial as do some of those on the back. It does not seem as though some of those lesions on the front of the chest are the same as those on the back. Obviously, on the forearm there are some remnants of an impetigo, but some of the lesions on the front of the chest look more like permanent infiltrations than do those due to pigmentary urticaria. The others are typical when properly brought out; it is too bad that we cannot study these histologically and compare what appear to me to be two clinically different types of lesions.

BROOKLYN DERMATOLOGICAL SOCIETY

E. ALMORE GAUVAIN, M.D., *Secretary*

Regular Meeting, Feb. 20, 1928

LOUIS CHARGIN, M.D., *President*

LICHEN NITIDUS. Presented by DR. THRONE.

C. S., a girl, aged 14, gave the history of a condition of three months' duration. It consisted of lichenoid papules, appearing on the lower part of the neck and upper part of the chest; some were arranged in irregular groups, which were rounded or oval; others were scattered around and between the groups. The individual papules varied in color from that of the normal skin to a light red and in size from that of a cross-section of a pin to that of a normal lichen planus papule. The skin covering the papules was in places normal; in others, red; and in the region of the older groups of lesions, pigmented. In the pigmented areas the skin seemed thinned, but no definite atrophy was discernible. The papules were flat topped. There were a few lesions of recent development on the thighs. The limbs never showed any involvement.

The biopsy report was as follows: The section showed a papule close under an atrophic epidermis. To either side of the infiltration the rete pegs appeared normal. Blood vessels in the upper corium were dilated and there was some interstitial and cellular edema. The cells in the papule were lymphocytes in an edematous stroma. There were pigmented cells with fine pigment, apparently chromatophores. There was also pigment in the stratum mucosum cells. In portions of the area of infiltration, there were dilated capillaries.

DISCUSSION

DR. ABRAMOWITZ: I am inclined to consider the condition as dermatitis lichenoides chronica atrophicans (Csillag). Although the lesions of lichen nitidus have been described recently as occurring in various parts of the body, they are almost pure white and never show the inflammatory appearance that the lesions in Dr. Throne's patient presents.

DR. WALZER: I agree with Dr. Abramowitz. I do not think any one, however, is able to classify these conditions definitely as yet. The present tendency is to regard lichen nitidus as tuberculous. The peculiar distribution in this case, the various shades of color, pigment and other features suggest to me dermatitis lichenoides chronica atrophicans rather than lichen nitidus.

DR. SKEER: The single papules appeared white, and if lichen nitidus is being taken into consideration as a diagnosis, I think a roentgenogram should be made of the chest to locate some other focus of infection that may prove to be tuberculous.

DR. THRONE: I think the diagnosis of dermatitis lichenoides chronica atrophicans suggested by Dr. Abramowitz can be ruled out entirely by the his-

tologic picture. In early lesions of lichen nitidus, as stated by Barber and by Arndt, the histologic picture is identical with that shown by this patient; it is not necessary for the section to show a tuberculous structure.

This case corresponded to the type described by Barber resembling pityriasis rosea. Barber stated that it was not necessary for the papules to be white or colorless, and he described them as showing the different shades of red or pink.

LUPUS ERYTHEMATOSUS, ACNITIS AND PAPULONECROTIC TUBERCULID. Presented by DR. ALTMAN.

Y. J., an unmarried girl, aged 18, a bookkeeper, had had an eruption for about eight years, which began on the side of the nose as a small papule and developed progressively. Four years later, the patient developed lesions on the scalp, arms and legs. She had been under treatment continuously and was first seen at the clinic of the United Israel Zion Hospital, Feb. 7, 1928.

At that time the scalp showed extensive scarring, loss of hair and erythematous scaly patches over both parietal regions. Over the malar prominences and on the nose there were pinkish-red, pea-sized confluent patches, which were covered with white gray and grayish-yellow scales. Over the left biceps region and along the ulnar surfaces of both arms were pea-sized to bean-sized atrophic areas. There was also marked livedo of the hands, with small papulonecrotic lesions and numerous varioliform scars over the patellae with crusted lesions over the achilles tendon. A few weeks before presentation pinhead and pea-sized, discrete, papulopustules developed on the forehead. These underwent necrosis and left varioliform scars. The patient had received two injections of a gold preparation and was beginning to improve.

DISCUSSION

DR. THRONE: This girl came to my clinic at the Skin and Cancer Hospital about six years ago. At that time the lesions on the face and scalp were acutely inflamed and suggested lupus vulgaris erythematoides of Leloir. A biopsy was not allowed. The blood gave a positive tuberculous complement-fixation test. The lesions of papulonecrotic tuberculid type were marked. I do not believe that lupus erythematosus of the chronic discoid type is ever caused by tuberculosis. There is no reason why a patient should not show tuberculous and nontuberculous lesions at the same time.

I have never seen tuberculous conditions respond to gold therapy. My experience here is limited to three cases of lupus vulgaris, one case of tuberculosis verucosa cutis, two cases of erythema induratum, two cases of papulonecrotic tuberculid, one case of lupus pernio of the Besnier type and one case of angiolupoid.

In regard to Bazin's disease, it has been stated that two types of this condition are seen, one in which there is a temporary remission of symptoms and another which does not show remissions. It may be that cases reported as responding to treatment with gold preparations belong to the first class, and that a relapse may occur later.

DR. WALZER: The interesting feature is the treatment. I have seen several cases in which the papulonecrotic condition cleared up and the lupus did not. This is not the usual result in treatment with gold preparations.

DR. BEST: Speaking of treatment with gold preparations, you will recall that I presented at the May meeting a patient who had erythema induratum of three years' duration. I gave her ten injections of a gold compound, starting with 50 mg. and increasing the amount to 100 mg. She did not develop any new lesions during the summer, and by the end of September, for the first time in three years the lesions were completely healed. I saw her again in January, and new lesions had not appeared since that time. I hope to present the patient again next May, and we shall see whether at the end of a year she has remained well.

DR. ABRAMOWITZ: The frequent occurrence of true tuberculous lesions of the skin with lupus erythematosus is a clinical fact in favor of tuberculous origin that is difficult to disprove. I do not deny that it may be due to other causes than tuberculosis. In my own experience, I have cured a severe case of lupus vulgaris and also a refractory case of Bazin's disease. A few similar cases have been reported by others, and therefore gold therapy should never be denied such patients even though the results are not always uniform.

DR. SKEER: I think this is an interesting case. In cases of papulonecrotic tuberculid, one rarely sees such large lesions. As to the question of the benefit of gold therapy in lupus erythematosis, one of our patients is responding very well from the administration of this drug. She had distinct red, infiltrated lesions, and, after two injections, the lesions faded to a marked degree. I think that the presenter of this case should include lupus pernio in his diagnosis, as the hands definitely show involvement. Lupus erythematosus is considered by a great many to be a toxemia due to endotoxins of the tubercle bacilli or some other germ.

DR. ALTMAN: We have treated several such patients at the clinic with gold compounds and have had good results. With the progress shown in this instance after but two injections I see no good reason why the patient should not progress nicely and why I cannot show her later in a much better condition.

DR. CHARGIN: My experience is similar to that of Dr. Throne. I have not treated as many patients as has Dr. Throne, but one case which I have in mind will serve as an example. This woman had an extensive papulonecrotic tuberculid on the arms, legs, face and back. She was treated with arsphenamine without any beneficial result. More recently she had received more than twenty gold and sodium thiosulphate injections, also without any beneficial results; in fact, while under treatment, an acute outbreak occurred. In two cases of Bazin's disease, little benefit was observed.

DERMATITIS EXFOLIATIVA (WILSON-BROCQ). Presented by DR. BEST.

C. R. R., aged 50, born in the United States, married, a hardware stock clerk, had a condition which began in April, 1927, and which consisted of two red areas, one on the right thigh and one on the left arm, which soon became scaly; these areas spread by peripheral extension. Simultaneously similar areas appeared on the trunk and extremities. During an interval of about two months the areas spread and coalesced, producing a generalized red, scaly eruption of almost the entire integument. When the rash became generalized, the itching become more pronounced. He stated that he felt chilly continuously, and that the skin felt tight. He had lost about 25 pounds (11.3 Kg.) in weight. Previously his health had always been good. The family history was negative. When presented, there was a dusky red, infiltrated and thickened skin over the entire body, except on the face and the scalp, which was dry and scaly. The scales varied in size from that of a lentil to twice that size; they were lamellated, and for the most part centrally attached, except on the face and scalp, where the scales were fine. The lower extremities were markedly swollen and there was some exudation of a mucilaginous character from these parts. Loss of hair was not noted, although the hair on the scalp was thin, but it had been so for years. The eyebrows were normal. There was a general adenitis. Laboratory examination revealed a trace of albumin in the urine; otherwise it was normal. The Wassermann test was negative. The blood count showed: hemoglobin, 75 per cent; red blood cells, 4,500,000; white blood cells, 9,000; polymorphonuclears, 75; small mononuclears, 15; large mononuclears, 1; transitionals, 2; eosinophils, 7 and a normal morphology. The chemical examination of the blood showed: sugar (Meyers method) 111, (Benedict method) 123; urea, 25; creatinine, 1.1; calcium, 9.9.

DISCUSSION

DR. ABRAMOWITZ: Many of us have come to believe that a patient is in a serious condition when he develops a generalized erythematous scaly eruption. The

primary lesion in such cases may be the inciting cause. One cannot place too much confidence in a normal blood count; later these patients may show a leukemic picture.

DR. WALZER: Whether it is primary or secondary is of course hard to determine. I think all of these cases are secondary. While the condition is now a dermatitis exfoliativa, I consider this purely a sympatomatic diagnosis; it is not a diagnosis of the underlying condition. After exfoliation disappears, we will call the condition something else.

An erythema that is progressing and developing infiltration and that persists for a long time, as has occurred in this case, has a poor prognosis.

DR. SKEER: About two years ago, the patient went to work in a hardware store, and after eleven months there he first noticed this condition of the skin. The skin is thick, markedly indurated and covered with scales. I think the condition is dermatitis exfoliativa, possibly due to arsenic, or some other heavy metal such as lead or mercury.

DR. THRONE: I was not on service when this patient came to the Skin and Cancer Hospital. I think that in the next year or two we will be able to clear up the causes of cases like this one. We are studying the relationship of the heavy metals to such conditions. The exfoliating dermatitis caused by arsphenamine and by mercury is well known. Bismuth, gold and probably lead can cause similar conditions, as can the inorganic or pentavalent arsenic. At the Strassburg reunion last June, Watrin reported a case of lichen planus of eight or nine years' duration in which the eruption spread widely after injections of arsenic and which did not respond to irradiation of the cord. Examination of the blood showed marked acidosis. Large doses of sodium bicarbonate by mouth and injections of sodium thiosulphate caused a resolution of the skin lesions, but the lesions of the mucous membrane were not affected. This acidosis, according to Ambard, is something new in medicine. We expect to study it in the near future. It is this which at times prevents the action of sodium thiosulphate in the treatment of patients with such conditions as this patient shows.

DR. BEST: Dermatitis exfoliativa due to arsphenamine is an acute process and may clear up after a reasonable time. This patient presents a marked infiltration, which means a chronic inflammatory process. He has lost considerable weight and shows signs of physical deterioration, so undoubtedly the condition of the skin is part of a general systemic disturbance. The blood picture rules out leukemia cutis unless it is of the aleukemic type. I cannot reconcile the present picture with pityriasis rubra of Hebra, which shows atrophy rather than infiltration and finer scales. For the present, I do not think we can make any other diagnosis than a primary dermatitis exfoliativa of the Wilson-Brocq type, due to a general toxemia which is also causing a general breakdown in his health. Ultimately, he may develop pityriasis rubra of Hebra.

BROMODERMA (?) Presented by DR. BEST.

A. J., colored, aged 20, married, a waitress, born in this country, was admitted to the genito-urinary service of Kings County Hospital on Dec. 11, 1927, with disease of the bladder (hematuria and frequent painful urination). About December 20, a rash appeared on the lower extremities below the knees. The lesions were solid, flat elevations of the skin, about the size of a split pea or slightly larger. Some of these lesions coalesced. No itching or discharge from the lesions was reported by the patient. Bromides had been ingested before admission to the hospital. When the patient was presented, there were the flat, verrucous-like, soft lesions, varying in size from that of a split pea to that of a five cent piece on both lower extremities between the knees and the ankles. The lesions were irregular, round, discrete and coalescent. Coalesced lesions formed irregular patches. The laboratory examination revealed: a moderate amount of albumin in the urine, red blood cells, *Bacillus coli* and streptococci. The Wassermann test was negative. A chemical examination of the blood showed: sugar, 82; urea, 22; creatinine, 1.

DISCUSSION

DR. GAUVAIN: This patient, when first seen on admission to the hospital and in consultation with the urologic department, had large pustular bullae on the anterior surfaces of both legs. Had she been well enough at the time of the last meeting, we would have had her here to exemplify a perfectly typical case of bromoderma.

DR. ABRAMOWITZ: If it is a bromide rash, it is important that chemical tests be made of the urine to confirm the diagnosis.

DR. WALZER: I agree with the diagnosis of bromoderma.

DR. THRONE: I agree that the diagnosis of bromoderma applies in this case.

ARSPHENAMINE ERUPTION (FIXED TYPE). Presented by DR. CHARGIN.

A. G., unmarried, a tailor, aged 29, had had syphilis for eight years, and during that period had received approximately fifty-five injections of arsphenamine and about 100 injections of bismuth and mercury. Although he occasionally developed an immediate reaction, he did not show any arsphenamine eruption until after he had had about thirty-five injections, after which he began to develop an eruption which appeared several hours after the treatment with arsphenamine. The eruption was limited in extent, mostly circular and red at first; later it became pigmented. There was accompanying itching at the site of eruption.

The eruption recurred after every treatment with arsphenamine. The old lesion would light up and become somewhat larger, and a few new spots would appear from time to time. The pigmentation persisted throughout an interval of two years.

DR. ABRAMOWITZ: This fixed rash is a rare type produced by the arsphenamine compounds. Would Dr. Chargin be kind enough to report whether the administration of silver arsphenamine to the patient would also cause this kind of an eruption?

DR. THRONE: I have seen only one other case like this. It was identical with the case shown except that more lesions were present.

DR. CHARGIN: It is our impression that we were the first to call attention to this type of arsphenamine eruption. We have tested several of these cases with phenolphthalein without producing any eruption, but we were always able to bring out an attack with arsphenamine, even after a rest period of a year in one instance. Antipyrin, quinine and acetylsalicylic acid, in addition to phenolphthalein, may bring out the type of eruption shown in this case.

TINEA CAPITIS (ADULT). Presented by DR. BERKOWITZ.

L. H., a white woman, married, aged 58, showed on the scalp one quarter-sized and two smaller circular patches covered with fine, yellowish scales which were rather adherent, and showed broken and stubby hair. Microscopic examination showed the presence of mycelia and spores. Several children in the family had ringworm of the scalp.

DR. THRONE: This is the first case of tinea capitis I have ever seen which was acquired in adult life.

Directory of Dermatologic Societies

NATIONAL DERMATOLOGIC SOCIETIES*

AMERICAN DERMATOLOGICAL ASSOCIATION

Otto H. Foerster, President, 445 Milwaukee St., Milwaukee.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.

SECTION ON DERMATOLOGY AND SYPHILOLOGY, SCIENTIFIC ASSEMBLY, AMERICAN MEDICAL ASSOCIATION

Jay Frank Schamburg, Chairman, 1402 Spruce St., Philadelphia.
William H. Guy, Secretary, Jenkins Arcade, Pittsburgh.
Place: Portland, Ore. Time: July 8-12, 1929.

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY (CANADIAN BRANCH)

D. King Smith, President, 122 Bloor St. West, Toronto.
E. J. Trow, Secretary, 122 Bloor St. West, Toronto.

LOCAL DERMATOLOGIC SOCIETIES

DERMATOLOGIC SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION

Irving R. Bancroft, Chairman, 412 W. 6th St., Los Angeles.
Louis F. X. Wilhelm, 1401 S. Hope St., Los Angeles.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Harry E. Alderson, Chairman, 490 Post St., San Francisco.
Ernest K. Stratton, Secretary and Treasurer, 490 Post St., San Francisco.

ATLANTA DERMATOLOGICAL SOCIETY

Cosby Swanson, President, 436 Peachtree St., Atlanta, Ga.
Howard Hailey, Secretary, Candler Bldg., Atlanta, Ga.

CHICAGO DERMATOLOGICAL SOCIETY

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Ralph Hopkins, President, 124 Baronne St., New Orleans.
Thomas A. Maxwell, Secretary-Treasurer, 1119 Union Indemnity Bldg., New Orleans.

BALTIMORE AND WASHINGTON DERMATOLOGICAL SOCIETY

C. Augustus Simpson, President, 1610, 20th St., N. W., Washington, D. C.
Leon Ginsburg, Secretary, 1800 N. Charles St., Baltimore.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

DETROIT DERMATOLOGICAL SOCIETY

George Van Rhee, President, 10 Peterboro St., Detroit.
Ralph A. Perkins, Secretary, 276 Erskine St., Detroit.

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Raphael Breakstone, Secretary-Treasurer, 783 Beck St., New York.

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Louis Chargin, President, 47 Halsey St., Brooklyn.
E. Almore Gauvain, Secretary-Treasurer, 47 Halsey St., Brooklyn.

MANHATTAN DERMATOLOGICAL SOCIETY

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